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ADULT COELIAC DISEASE AND OTHER DISORDERS ASSOCIATED WITH STEATORRHOEA*

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A disturbance of function of the small intestine which is readily demonstrable is the presence of excess fat in the faeces (steatorrhoea), and the abnormality is common to a number of disorders. To these a blanket term, such as "malabsorption syndrome" (Cross *et al.*, 1953), "sprue syndrome," "steatorrhoea syndrome," "jejuno-ileal insufficiency" (Bennett and Hardwick, 1940), or "sprue" has been applied. This nomenclature has achieved much popularity in clinical usage, but, like many such terms in medicine for conditions of unknown aetiology, is too often regarded as a complete diagnosis. They are misleading and are apt to cause significant aetiological differences to be overlooked. For example, "malabsorption syndrome" is not usually applied to pernicious anaemia, but is to idiopathic steatorrhoea (adult coeliac disease), which is generally regarded as being due to malabsorption, though future research may implicate malutilization also.

Classification

The clinical disorders that have steatorrhoea as part of their presentation fall into three main groups. The first group is associated with disturbances of conditions or processes of digestion within the lumen of the bowel following upon upsets of gastric, pancreatic, biliary, or intestinal function, such as post-gastrectomy states, obstructive jaundice, intestinal resection, or entero-anastomoses. The second group is associated with the presence of pathological changes in the wall of the bowel, regional ileitis, non-specific or infective enteritis, intestinal lipodystrophy, tuberculosis, lymphoma, scleroderma, neoplasm, or amyloid disease. Disorders of the mesenteric lymph nodes or retroperitoneal tissues—for example, tabes mesenterica or lymphoma—have sometimes been placed in a separate group (disturbances of the distributive tissues), but there is no evidence to show that such disorders are associated with steatorrhoea unless the intestinal wall itself is involved.

There remains the third group of disorders, in which there is no obvious contributing factor: tropical sprue, coeliac disease, and non-tropical sprue, or idiopathic steatorrhoea. Clinical evidence is strong that coeliac disease and idiopathic steatorrhoea are basically the same disorder, partly on account of the similar reactions to gluten-free diets (van de Kamer *et al.*, 1953; French *et al.*, 1957) and partly on account of the high incidence of previous coeliac disturbance in adult patients presenting with idiopathic steatorrhoea (Cooke, Peeney, and Hawkins, 1953).

Many consider that tropical sprue and non-tropical sprue are as closely connected. For example, Thaysen (1932) writes that the symptoms and signs of both disorders were so similar that they must be considered the same disease, whilst Bossak *et al.* (1957) thought that they were clinical manifestations of the same underlying metabolic disorder. Not infrequently observations are recorded from both conditions and discussed as though the patients were all suffering from the same disorder (Bossak *et al.*, 1957; Butterworth *et al.*, 1957; Butterworth and Perez-Santiago, 1958). However, as is pointed out below, in the absence of any known aetiology for either, there are observations which suggest that they might be more profitably regarded as separate entities. Therefore it would be wise to reserve "tropical sprue" for the disorder arising in tropical or semi-tropical countries and to use a distinctive term for the disorder encountered in temperate climates.

Adult coeliac disease is such a term, discarding both the title most favoured in the United States—"non-tropical sprue"—with its implied aetiological association with tropical sprue, and that most favoured in England—"idiopathic steatorrhoea"—with the implication that steatorrhoea is of primary importance and always present. It is therefore the purpose of this paper to consider critically the non-specific character of many clinical and laboratory findings in patients with steatorrhoea whilst emphasizing features which suggest that adult coeliac disease is a distinct clinical entity.

In any individual patient it is unfortunate that symptomatology or even physical examination gives little lead to differentiation, though the presence of an abdominal scar suggests a possible surgical cause for the steatorrhoea. Nevertheless, adult coeliac disease does possess a clinical picture which will often allow a diagnosis to be reached, albeit in many instances by a process of exclusion. Characteristic features are chronic ill-health, recurrent glossitis, disorders of haemopoiesis, and certain radiological findings, in addition to steatorrhoea (Cooke, Peeney, and Hawkins, 1953). It is on these three investigations that the main points in differential diagnosis have been based in the past.

Steatorrhoea

Other functions of the small intestine may be disturbed, but steatorrhoea remains the only satisfactory finding upon which to base a diagnosis, even though it may not necessarily be present always in adult coeliac disease. The mere determination of the percentage fat in a single specimen of dried faeces is now recognized to be of little use. The

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introduction of balance techniques in which the amount of fat ingested was compared with that excreted, and the results expressed in terms of percentage absorption, led to an appreciation of the frequency of steatorrhoea (Cooke *et al.*, 1946). The use of measured intakes created difficulties, and with increasing experience it became evident that normal subjects on diets containing between 50 and 150 g. of fat rarely excreted more than 6 g. a day; indeed, the mean was usually between 3 and 4 g. (Wollaeger *et al.*, 1947; Crowe and Blackburn, 1956). It has thus become possible to dispense with rigid dietary measurements and use normal mixed diets either in hospital or at home. For diagnostic purposes it is adequate to collect the stools for 3 to 6 days without markers, using the method of fat analysis introduced by van de Kamer *et al.* (1949).

It was for long traditional that increase in the ratio of neutral fat to split fat was diagnostic of pancreatic disorders, but this determination is rarely done now, since such interpretations have been demonstrated as incorrect (Cooke *et al.*, 1946). Similarly, increase in faecal nitrogen is a reflection more of the degree of steatorrhoea or inflammation of the alimentary tract than of the presence of pancreatic dysfunction (Comfort *et al.*, 1953; Cooke, Thomas, *et al.*, 1953). According to Dreiling (1953), only about 20% of patients with pancreatitis have steatorrhoea, and certainly if there is gross steatorrhoea in such patients virtual absence of pancreatic function can be predicted.

Much has been made of tagged iodinated fats for detecting steatorrhoea (Chinn *et al.*, 1952; Beres *et al.*, 1957). For those with suitable counting apparatus these methods are convenient and simple. Unfortunately the reports indicate that the results do not give a satisfactory correlation with chemical balances in a significant number of patients (McKenna *et al.*, 1957). The source of the excess fat in the faeces has been much debated, and it is evident that fats are excreted into the intestinal tract (Sperry and Angevine, 1932; Kim *et al.*, 1956), but, except in occasional patients (Comfort *et al.*, 1953; Cooke, Thomas *et al.*, 1953; Weijers and van de Kamer, 1953), steatorrhoea is due principally to unabsorbed dietary fat. As an additional possibility, Frazer and Sammons (1956) claim to have isolated fat-forming bacteria from the stools of patients with tropical sprue, but as yet their observations have not been confirmed or repeated.

Radiology

No patient with steatorrhoea can be adequately investigated without a careful radiological examination of the small intestine. Such investigations are time-consuming and expensive, demanding the fullest co-operation between the radiologist and his clinical colleagues. The type of barium suspension used is a matter of preference, but, on balance, the poorly flocculating type of barium seems preferable at the first examination, since mucosal pattern, areas of dilatation, or strictures are more easily delineated. Jejunitis, jejuno-ileitis, scleroderma, intestinal diverticulae, blind loops, entero-anastomoses, and adult coeliac disease may often be differentiated even though the clinical picture in each condition may be somewhat similar (Adlersberg *et al.*, 1954). As Ardran *et al.* (1950) demonstrated, excess mucus is the cause of flocculation of a barium-and-water suspension. Though this is seen frequently in adult coeliac disease, flocculation of barium does occur in other conditions in which there is no steatorrhoea, as, for example, in some patients with pernicious anaemia, nephrosis, or hypoproteinaemia. It has been suggested that there are few if any disturbances of radiological pattern in pancreatic steatorrhoea and that this was of diagnostic significance (Bjerkelund and Husebye, 1950; Salvesen and Böe, 1953; Marshak and Eliasoph, 1957). However, while there are usually no significant abnormalities to be seen radiologically, except in those patients with pancreatic lithiasis, flocculation and dilatation are encountered often enough to make radiological diagnosis of pancreatitis unreliable.

Haematology

Patients with steatorrhoea may develop anaemia due to any or all of three main causes: deficiency of iron, cyanocobalamin (vitamin B_{12}), or folic acid. It is likely that anaemias due to copper (Cartwright, 1955) or pyridoxine (Harris *et al.*, 1956) deficiency occur also, but as yet none have been reported. The characteristic peripheral blood picture is that of macrocytosis with poorly staining haemoglobin and often many small cells, though not so small as noted in true iron-deficiency anaemia (Cooke *et al.*, 1948). A patient with steatorrhoea who persistently maintains a normal blood picture is unlikely to be suffering from adult coeliac disease. A more probable explanation is pancreatic atrophy, in which, except in states of marked malnutrition, anaemia is rare.

In adult coeliac disease, Badenoch and Callender (1954) demonstrated that radioactive iron was poorly absorbed. Despite this, patients will be encountered in whom the iron deficiency will readily respond to oral iron administration. More often, however, parenteral administration will be necessary to restore the blood picture, and the finding of macrocytosis following such therapy can be regarded as suggestive evidence of adult coeliac disease (Hawkins *et al.*, 1950). Though iron seems to be poorly absorbed, in some patients at least there seems to be an additional factor of poor utilization. Also patients with regional ileitis are particularly prone to iron-deficiency anaemia, which is often difficult to correct by oral iron administration. In some instances this can be demonstrated as being due to long-continued loss of blood from the intestine (Ensrud *et al.*, 1957).

It has often been suggested that intestinal lipodystrophy is associated with hypochromic anaemia (Plummer *et al.*, 1950), due in some degree to the persistent loss of blood into the intestinal tract. However, hypochromic anaemia alone is by no means invariable, as perusal of the literature will reveal a number of patients with macrocytic anaemia, observations supported by experience in Birmingham.

Vitamin B_{12} is absorbed principally from the lower end of the small intestine, and four main causes give rise to low serum vitamin B_{12} levels. The first is that due to loss of intrinsic factor and is seen in the post-gastrectomy group of steatorrhoeas. The second is thought to be due to utilization of vitamin B_{12} by the intestinal bacteria, and is seen in the macrocytic anaemias of the intestinal diverticula (Callender and Evans, 1955; Halsted *et al.*, 1956). Whether this is the correct explanation of the condition is perhaps debatable; in practice, the administration of antibiotics, in particular chlortetracycline, leads to correction of the anaemia (Dick, 1955). It is noteworthy that the antibiotic which has its major effect within the intestinal lumen—neomycin—has no effect (Doscherholmen and Hagen, 1954; Halsted *et al.*, 1956). The third cause appears to be an intracellular defect righted by steroid therapy, and is encountered in both adult coeliac disease and regional ileitis (Callender and Evans, 1955; Meynell *et al.*, 1957). Oxenhorn *et al.* (1957) found that 20 out of 25 patients with adult coeliac disease had diminished absorption of radioactive vitamin B_{12}, which was unaffected by either intrinsic factor or administration of antibiotics. In practice approximately 50% of patients with adult coeliac disease will have low serum vitamin B_{12} levels (Meynell *et al.*, 1957). In regional ileitis 60% of patients have been found to have low levels (Meynell *et al.*, 1957) due to failure of absorption of vitamin B_{12}, which is improved by steroid therapy. It is evident, therefore, that some patients with regional ileitis may simulate those with adult coeliac disease with steatorrhoea, megaloblastic anaemia, and nutritional changes, but differentiation is possible by radiological examination of the intestine. The last cause is resection of the ileum, as, for example, in the treatment of regional ileitis (Oxenhorn *et al.*, 1957).

In adult coeliac disease abnormalities in folic acid excretion following oral administration have been demonstrated as an almost invariable finding (Girdwood, 1953

1956; Cox *et al.*, 1958a). It is not surprising that many patients have a macrocytic anaemia due to both folic acid and vitamin-B_{12} deficiency. Folic acid is, however, absorbed in the jejunum (Cox *et al.*, 1958a). Consequently, the clinical picture and laboratory findings of adult coeliac disease may be simulated by some patients with jejunitis or jejunoileitis. Such patients may easily remain undiagnosed owing to the significance of the radiological pattern being overlooked. Furthermore, this condition may undergo complete resolution. Indeed, it may be questioned whether these patients are not the real non-tropical counterpart of patients with tropical sprue in which the folic acid defect is often considered the earliest manifestation.

In an endeavour to discover a specific diagnostic test for adult coeliac disease, a number of procedures have been introduced, but few have stood the test of time or proved to be more than a screening test. Glucose-tolerance tests have been a traditional diagnostic aid, but flat curves are now considered to have no great diagnostic significance, since 13 to 30% of the normal population may have such curves (Gardner, 1956; Test *et al.*, 1956). Furthermore, patients who by all other criteria have adult coeliac disease may have completely normal glucose-tolerance tests (Cooke, Peeney, and Hawkins, 1953). On the other hand, a grossly lowered tolerance test may well be evidence of pancreatitis. King (1949), from a review of the literature, concluded that 35 to 50% of patients with chronic relapsing pancreatitis had diabetic blood-sugar curves.

Should diabetes mellitus supervene in adult coeliac disease as has been reported (Bossak *et al.*, 1957), other tests, such as the folic-acid or xylose-excretion test, must be used. However, it is only too evident that as a diagnostic test there are so many different factors to be considered in the interpretation of the curves that other tests of carbohydrate absorption have been developed. A test of promise is the *d*-xylose-excretion test (Fourman, 1948; Gardner and Santiago, 1956; Benson *et al.*, 1957) in which the amount excreted in the urine in five hours after the administration of 25 g. of xylose is measured. The test is readily repeatable and the estimation is useful in differentiating between those patients with adult coeliac disease, or the active phase of tropical sprue, and those with pancreatic steatorrhoea, though a wide range of results may be encountered in other disorders with steatorrhoea.

As part of routine investigation serum calcium and phosphorus are usually estimated. Low values for both are often encountered in adult coeliac disease, but essentially similar findings are found in some patients with chronic recurrent pancreatitis (Sterkel and Kirsner, 1958), enteroanastomoses, gastro-colic fistulae, or severe post-gastrectomy steatorrhoeas. The values may also be suggestive, if not diagnostic, of certain rare clinical conditions associated with steatorrhoea: a high calcium and low phosphorus serum values may indicate the association of hyperparathyroidism and chronic pancreatitis (Davies *et al.*, 1956; Plough and Kyle, 1957), with or without jejunitis. Low calcium and high phosphorus levels in the serum are more uncommon, and may indicate hypoparathyroidism (Salvesen and Böe, 1953), often associated with moniliasis (Collins-Williams, 1950) or pseudohypoparathyroidism (Lowe *et al.*, 1950).

Amongst other screening tests should be mentioned the fasting carotene serum level, vitamin-A-absorption tests, and chylomicrographs (Barnes *et al.*, 1950; Adlersberg *et al.*, 1957; Wenger *et al.*, 1957). None are consistent; they bear a closer correlation to the degree of malnutrition than to the diagnosis, and will often produce abnormal results in disorders not associated with steatorrhoea. The main use of such tests is to indicate, in the event of abnormality, that steatorrhoea must be excluded, but, should they be normal, steatorrhoea may still be present. Intubation studies in patients with steatorrhoea are not particularly helpful in differential diagnosis. Whilst the concentration and amounts of pancreatic enzymes are usually normal in adult coeliac disease (Cooke, Peeney, and Hawkins, 1953; Bossak *et al.*, 1957) the presence of deficient pancreatic secretion may only indicate chronic malnutrition (Jackson and Linder, 1953). For differentiation between adult coeliac disease and pancreatogenous diarrhoea, either the xylose- or the folic-acid-excretion test is more simple. However, in the majority of patients it should be possible to make a fairly accurate diagnosis with haematological and careful radiological investigation only.

There are, however, three further procedures which add greater accuracy to the diagnosis and suggest that adult coeliac disease has certain distinctive features.

Intestinal Biopsy

The development by Margot Shiner (1956, 1957) of a satisfactory technique for biopsy of the jejunal mucosa has added further refinement to diagnosis. Though much more data still remain to be collected and critically assessed, it is clear that histological changes are to be found in the intestine and that previous reports of abnormalities based on post-mortem evidence (Adlersberg and Schein, 1947; Oehler, 1953) cannot be completely dismissed. Mucosal, mainly villous atrophy affecting the jejunum and ileum is the characteristic feature of adult coeliac disease, and no patient in whom this diagnosis seemed probable on other grounds has been found to have a normal jejunal mucosa. Whether such atrophy is diagnostic of adult coeliac disease is not so certain; indeed, occasional patients following gastrectomy may have a somewhat similar though less marked atrophy (Baird and Dodge, 1957). Butterworth and Perez-Santiago (1958) describe jejunal biopsies of "sprue" as showing enlarged oedematous coalescent villi, the epithelium having increased numbers of globular cells and some fibrosis and inflammation in the subepithelial layers. Another entity is emerging in which histological changes of inflammation and atrophy suggest the diagnosis of jejunitis, whilst at operation the gut may seem to be thickened and oedematous though not to the same degree that is usually seen in regional ileitis.

Clinically, steatorrhoea need not necessarily be present, since this will depend upon the extent to which the jejunum is involved. Folic-acid-excretion tests are, however, abnormal and a macrocytic anaemia responding to folic acid may develop. There is clinical evidence that some of these patients at least undergo complete cure. Whether any develop jejunal mucosal atrophy is not known, but clearly this is a possibility. Since these patients do not respond to a gluten-free diet, it is unlikely that the group have any direct relationship to adult coeliac disease. Intestinal biopsy therefore does provide some evidence that adult coeliac disease differs from tropical sprue, and tropical sprue may well prove to be analogous to the "jejunitis" encountered in non-tropical countries.

Folic-acid-excretion Test

Girdwood (1953) suggested that comparison of the amount excreted in the urine following the intramuscular injection of folic acid and that following oral administration could provide a relatively simple method for diagnosing steatorrhoea, since the amount excreted in patients following the oral dose was significantly less than that following the intramuscular. It is evident from both his original paper and his later observations (Girdwood, 1956) that he referred to adult coeliac disease rather than all the other disorders associated with steatorrhoea. His observations have been confirmed and extended, the folic-acid-excretion test being shown abnormal in adult coeliac disease, active tropical sprue (Butterworth *et al.*, 1957), and jejunitis, whilst being completely normal in pernicious anaemia, post-gastrectomy and pancreatic steatorrhoea, or any disorder in which the jejunum is not pathologically involved (Cox *et al.*, 1958a). With remission of symptoms in tropical sprue the folic-acid test returns to normal (Butterworth *et al.*, 1957). On the other hand, the attainment of "clinical cure" with a gluten-free diet and the disappearance of steatorrhoea are not necessarily associated with a return to normality of the folic-

acid-excretion test, for nine of the tests carried out in ten such patients remained abnormal (Cox *et al.*, 1958a).

The inference that has been drawn from an abnormal absorption test is that there is poor absorption from the intestinal tract. It can, however, be demonstrated that the excretion of folinic acid following both the intramuscular and the oral administration of folic acid is essentially the same (Cox *et al.*, 1958b). Since the excretion of folinic acid is known to be increased after the administration of folic acid, either the folic acid is absorbed so slowly and completely that the renal threshold of excretion is not exceeded, or there is some degree of malutilization of folic acid comparable to that postulated to occur with ascorbic acid in adult coeliac disease (Boscott and Cooke, 1954). This test, which has many important theoretical implications, is unlikely to be widely used, since it necessitates microbiological assay, and though the assay is relatively simple the number of occasions that it is likely to be required is few except in certain special centres. It is to be hoped that the xylose-excretion test can be made to provide equally useful data in differential diagnosis.

Gluten-free Diet

The third test is the therapeutic test with a gluten-free diet. Following its introduction by Dicke *et al.* (1953) and confirmation of its efficacy in coeliac disease in children (Anderson *et al.*, 1952) reports soon followed on its value in adult coeliac disease. In the largest and most recent study French *et al.* (1957) had clinical cures in 15 out of 22 patients who appeared to fulfil the criteria of adult coeliac disease. Most significant was their demonstration, in some patients, of a rapid haematological remission produced by the removal of gluten from the diet. The offending substance appears to be in the gliadin fraction of the gluten occurring in wheat or rye, and further analysis shows it to be polypeptide (Frazer, 1956).

From reports in the literature and from personal experience, it does seem justifiable to assume, should clinical cure result, that the patient was suffering from adult coeliac disease. The contrary assumption is not necessarily true. The effect of gluten appears to be quantitative, and even in patients in whom fat absorption has returned to normal the folic-acid-excretion test remains abnormal. The possibility therefore remains that there is a "constitutional enzymatic defect" which is rendered evident by gluten administration but which in some patients may be so gross that it cannot be corrected even by a gluten-free diet. From haematological effects and the persistently abnormal folic-acid excretions, gluten might be postulated as acting as a "blocking" agent of an underlying metabolic disorder, possibly of the pteroylglutamate complex. There may well be other substances, probably of protein nature, which act in a similar way. The effect of a gluten-free diet has been assessed in a number of conditions. The diet itself has a mildly constipating effect on normal subjects, and experimentally has been shown to decrease fat excretion in rats (Ribeiro *et al.*, 1957). However, no significant effect has yet been demonstrated in patients with tropical sprue (French *et al.*, 1957), regional ileitis, or pancreatogenous diarrhoea.

Conclusion

It is now apparent that tropical sprue, on the basis of the intestinal biopsy findings, the lack of response to a gluten-free diet, and the probability of the folic-acid test returning to normal, must be regarded as significantly different from adult coeliac disease. Jejunitis, which could on occasion simulate adult coeliac disease, can be shown to differ by the findings on intestinal biopsy and the invariable lack of response to a gluten-free diet, and may well prove to be the non-tropical counterpart of tropical sprue.

The condition that is known in this country as idiopathic steatorrhoea and in the United States as non-tropical sprue is now taking on more defined characteristics and deserves a distinctive name—adult coeliac disease—to replace the two previous unsatisfactory titles. In brief, it appears to be a familial constitutional disorder (Thompson, 1951 ; Cooke, Peeney, and Hawkins, 1953). Four observations suggest that this is an enzymatic defect and probably associated with folic acid metabolism. These are as follows: the rapid haematological remission in some patients on a gluten-free diet (French *et al.*, 1957) ; the abnormal folic-acid-excretion test (Girdwood, 1956 ; Cox *et al.*, 1958a) ; the rise of blood glutamine following gluten administration in some patients (Weijers and van de Kamer, 1953) ; and the abnormality in which pteroylglutamates may be involved and which lead to the persistent excretion of *p*-hydroxyphenylacetic acid, not easily eliminated by administration of ascorbic acid (Boscott and Cooke, 1954). As to where this enzymatic defect is sited—whether in the intestinal cell or liver—future research must show. It cannot, however, be too strongly emphasized that the actual absorptive functions of the intestinal cell are relatively minor compared with the major metabolic functions that it performs.

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GIANT-CELL GRANULOMA OF THE RESPIRATORY TRACT (WEGENER'S GRANULOMATOSIS)

BY

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This paper is based on a retrospective study of data from 10 patients who had in common an illness characterized by symptoms of progressive ulceration in the respiratory tract together with signs of widespread inflammatory disease. Histological examination of material from each case shows disseminated granulomata, most common in the respiratory tract and kidneys, and widespread vascular lesions similar to polyarteritis nodosa. The name Wegener's granulomatosis has been applied to this syndrome (Ringertz, 1947; Johnsson, 1948; Fahey *et al.*, 1954). The purpose of this paper is to describe in brief the clinical and pathological features, to give a concept of the pathogenesis, and to suggest a method of treatment. The cases, which were selected according to the pathological criteria of Godman and Churg (1954), have been described in detail elsewhere (Leggat and Walton, 1956; Walton, 1957).

Clinical Features

The main data from each case, and from 46 others selected from the literature, are summarized in Table I. An analysis of symptoms and signs is given in Table II. Typically, the disease occurs in previously healthy young or middle-aged adults of either sex. The onset is insidious, with non-specific symptoms of infection in some part of the respiratory tract. Two patterns can be distinguished. In about two-thirds of the cases persistent purulent rhinorrhoea is accompanied by nasal obstruction and crusting, antral pain, and epistaxis. Otorrhoea, deafness, or ulceration of the gums was the initial symptom in a few of these: each later developed rhinorrhoea. In the second, smaller group, attention is drawn to the lungs because of chronic cough, haemoptysis, or pleurisy. Often the constitutional upset is out of proportion to the apparent intensity of the local lesion, and the patient seeks advice because of persisting malaise, fever, or weakness.

The course is usually rapid and full of incident, progressing to death in, on average, five months, occasionally in as little as four weeks. A few patients (Cases 9, 19, 43, 45, and 47, Table I) have had a more chronic illness with periods of remission, and survival for up to four years. Though temporary improvement sometimes follows antibiotic treatment, the local lesion always persists. Spread of the inflammatory process leads to extensive mucosal ulceration and cartilaginous or osseous destruction in the nose and palate on the one hand, and to widespread pulmonary consolidation on the other. Spread through the upper air passages is often followed by conjunctivitis, dimness of vision, increased lacrimation, and exophthalmos, deafness, earache, and otorrhoea. The development of a sore mouth, hoarseness, or dysphagia has resulted in the discovery of ulceration in the fauces, pharynx, or larynx. Only twice (Cases 1 and 53) has the mucosal ulceration spread to involve the skin of the face.

Sooner or later signs of widespread inflammatory disease appear in every case: fleeting arthralgia, numbness and tingling in the limbs, sensory loss, muscle weakness or paralysis, and a haemorrhagic vesicular rash most frequent on the skin of the face, wrists, and elbows and the oral mucosa are all common. A pericardial friction rub or electrocardiographic changes occasionally indicate involvement of the heart; parotitis, orchitis, and prostatitis also occur. In the late stages fever, usually of septic type, is almost constant, and albuminuria, haematuria, cylinduria, and/or pyuria have indicated renal involvement in nearly every case.

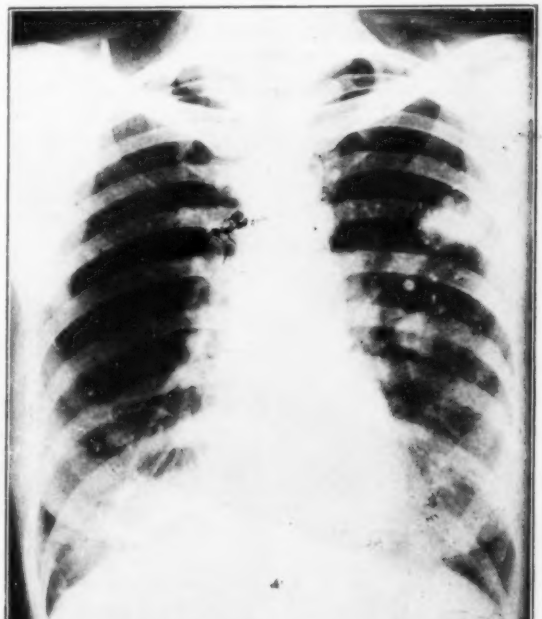

FIG. 1.—Case 10. Multiple rounded opacities are present in the left upper zone and both lower zones. Spicules of calcification are seen in the left upper zone.

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TABLE I.—*Clinical Features of 56 Cases of Wegener's Granulomatosis*

Case No.	Author	Description	Age and Sex	Onset	Duration Months	Initial Symptoms	Respiratory Tract Symptoms		Eye Changes	Ear Changes	Skin Rash	Joint Changes	Neuropathy	Other Organs	Urinary Changes	Cause of Death
							Upper	Lower								
1	Walton	Wegener's granulomatosis	39 M	1943	1½	Sore gums, limb pains	Epistaxis, rhinorrhoea	Cough	+	+	+	−	+	−	+	Respiratory failure
2	,,	,, ,,	33 M	1948	2½	Otorrhoea, nasal obstruction	Nasal block, epistaxis	Nil	+	+	+	−	−	−	−	? Uraemia
3	,,	,, ,,	34 F	1948	3½	Nasal block, joint pains	Purulent rhinitis	Stridor, dyspnoea	+	+	+	+	−	−	+	Respiratory failure
4	,,	,, ,,	42 F	1954	10	Pleurisy	Anosmia, oral ulceration	Productive cough	+	+	+	+	+	−	+	Circulatory failure
5	,,	,, ,,	62 M	1955	3	Dyspnoea	Nasal block, rhinitis	Dyspnoea			−	−	−	−	+	Uraemia
6	,,	,, ,,	52 M	1954	3	Deafness, sinusitis	Sore mouth	Cough, haemoptysis		+	−	+	−	−	+	Respiratory failure
7	,,	,, ,,	75 M	1955	1½	Cough, dyspnoea	Nil	Pain in chest	−		−	−	−	−	+	,, ,,
8	,,	,, ,,	56 M	1947	1	Malaise	,,	Nil	−	−	+	−	−	−	+	Uraemia
9	,,	,, ,,	73 M	1954	21 +	Cough, joint pains	Hoarseness, sore throat	Haemoptysis	+	+	+	+	−	+	+	(Alive)
10	,,	,, ,,	42 F	1955	12 +	Rhinitis with obstruction	Epistaxis	Productive cough	−	−	+	−	−	−	+	,,
11	Klinger (1931)	Periarteritis nodosa	70 M	1930	12	Sinusitis	Purulent rhinitis	Nil	+	−	−	+	−	−	+	? Uraemia
12	Rössle, 4 (1933)	Rheumatism	44 M	1931	9	Joint pains, septic illness	Rhinitis, dysphagia	,,	+	+	+	+	−	−	+	Uraemia
13	Wegener (1936)	Rhinogenic granulomatosis	38 M	1934	5	Jaw pain, rhinorrhoea	Saddle nose, hoarseness	,,		+	+	+	−	−	+	Respiratory failure
14	,,	,, ,,	36 F	1935	6	Rhinorrhoea	Foul rhinorrhoea	Productive cough	−	−	+	−	−	−	+	Uraemia
15	,,	,, ,,	33 F	1933	3	Sanious rhinitis, headache	Fetor, gum bleeding	Nil	−	−	−	−	−	−	+	,,
16	Postel and Laas (1941)	Periarteritis nodosa with lung changes	44 M	1939	4	Rhinorrhoea, epistaxis	Headache	Chest pain	−	−	−	−	−	−	+	,,
17	,,	,, ,,	42 F	1940	1	Otorrhoea	Earache	Nil	−	+	−	−	+	−	+	,,
18	Banowitch *et al.*, 5 (1942)	Periarteritis nodosa ,,	35 F	1936	8	Cough	Epistaxis	Productive cough	+	−	−	−	+	−	+	Cardiac failure
19	Staehelin (1942)	Sarcoidosis	20 F	1938	30	Dyspnoea, dysphagia	Sanious rhinitis, stridor	Purulent sputum	+	−	−	+	+	−	+	
20	Lindsay *et al.* (1944)	Chronic granuloma	67 F	1939	13	Saddle nose, epistaxis	Sanious rhinitis	Productive cough	−	−	−	−	−	+	+	Uraemia
21	Weinberg (1946)	Unknown granuloma and periarteritis nodosa	38 M	—	2	Sinusitis	Epistaxis, nasal block	Nil	−	−	+	−	−	−	−	Cardiac failure
22	,, ,,	,, ,,	50 F	—	—	Leg pains, sore throat	Nil	Cough, haemoptysis	−	−	+	−	+	−	+	Respiratory failure
23	Ringertz (1947)	Periarteritis nodosa; an unusual type	34 F	1945	8	Gum ulcer, cough	Nasal obstruction	Nil	−	−	−	−	−	−	+	Sepsis, cachexia
24	,, ,,	,, ,,	62 F	1947	3	Cough, fever	Nil	Productive cough	−	−	−	−	−	−	+	Uraemia
25	Johnsson (1948)	Wegener's granulomatosis	59 F	—	3	Deafness, earache	Otorrhoea	Nil	−	−	−	−	−	−	+	
26	Williams, 3 (1949)	Lethal midline granuloma	21 M	—	8	Sinusitis, fever	Epistaxis, otorrhoea	Chest pain, cough	−	+	+	−	−	−	+	Respiratory failure
27	McCart (1950)	Malignant granuloma	52 F	1948	4	Sinusitis	Sanious rhinitis	Nil	+	+	−	−	−	−	+	
28	,, ,,	,, ,,	52 M	1947	9	Rhinorrhoea, headache	Earache	,,	−	−	−	−	−	−	+	Uraemia
29	Howells and Friedmann (1950)	Giant-cell granuloma ,,	23 M	1949	5½	Rhinitis with obstruction	Gingivitis	,,	+	−	−	−	−	−	+	,,
30	Mallory (1950)	,, ,,	69 F	1950	5	Cough with sputum	Nil	Productive cough	−	−	−	−	+	−	+	
31	Pugh (1950)	Complications of sinusitis	— M	1950	4	Deafness and headache	Nasal obstruction	,, ,,	+	+	−	+	−	−	+	Respiratory failure
32	Woodburn and Harris, 1 (1951)	Idiopathic nasal granuloma	31 M	1942	21	Nasal obstruction	Epistaxis, aphonia, fetor	Nil	−	−	−	−	−	−	+	
33	Ahlström *et al.* (1953)	Respirato-renal type of periarteritis nodosa	70 M	1948	2	Chest pain, dyspnoea	Nil	Pain, dyspnoea	−	−	−	−	−	−	+	Uraemia
34	,, ,,	,, ,,	41 F	1948	14	Sinusitis	Crusting and hoarseness	Pneumonia	+	−	+	+	−	+	+	,,
35	Stratton *et al.* (1953)	Nasal granuloma and periarteritis nodosa	49 M	1951	3	Rhinitis with obstruction	Epistaxis	Nil	+	−	−	−	+	−	+	Cardiac failure
36	,, ,,	,, ,,	51 M	1951	6	,, ,,	Epistaxis, hoarseness	Cough	−	+	−	−	+	−	−	Uraemia
37	Fienberg (1953a)	Necrotizing granulomatosis of lungs	27 M	1950	7	Haemoptysis, chest pain	Epistaxis, stomatitis	Pain, haemoptysis	+	−	−	+	−	−	+	,,
38	,, ,,	,, ,,	54 M	1950	1½	Dyspnoea, cough	Nil	Cough, haemoptysis	−	−	−	+	−	−	+	Respiratory failure
39	Fahey *et al.* (1954)	Wegener's granulomatosis	40 F	1951	2	Sinusitis, atelectasis	Crusting	Nil	−	−	−	+	−	−	+	Uraemia
40	,,	,, ,,	34 M	1951	14	,, arthritis	Epistaxis	Nil	+	−	−	+	+	−	+	,,
41	,,	,, ,,	50 M	1950	3	Orchitis, weakness	Oral ulceration	Cough, chest pain	+	−	−	+	+	+	+	,,
42	,,	,, ,,	39 M	1949	5	Sinusitis	Rhinorrhoea	Nil	+	−	−	+	+	+	+	,,
43	,,	,, ,,	43 M	1933	48	Sinusitis, otitis	Hoarseness, saddle nose	,,	+	+	−	−	+	−	+	Septicaemia
44	,,	,, ,,	12 F	1953	1	Rhinorrhoea, sinusitis	Purulent rhinitis	Dyspnoea	+	−	+	+	+	−	+	Respiratory failure
45	,,	,, ,,	38 M	1951	39	Sinusitis, cough, pleurisy	Saddle nose	Nil	+	−	−	−	+	−	+	Uraemia
46	McCallum (1954)	Nasal granuloma, periarteritis	31 M	1952	2	Sinusitis, fever	Purulent rhinitis	Chest pain	+	−	−	+	+	−	+	,,
47	Seidelin and Willcox (1954)	Giant-cell granuloma and periarteritis nodosa	55 F	1944	40	Sanious rhinorrhoea	Oral ulceration	Nil	+	−	−	+	−	−	+	
48	,, ,,	,, ,,	54 M	1949	17	,, ,,	Nasal deformity	,,	−	−	−	−	+	−	+	Cardiac failure
49	,, ,,	,, ,,	59 F	1947	9	Bleeding from ear	Sinusitis	,,	+	+	−	−	+	−	+	Uraemia
50	Milner (1955)	Giant-cell granuloma	41 F	1954	2	Swollen gum, rhinitis	Dysphagia	,,	+	−	+	−	−	−	−	,,
51	Cogan, 2 (1955)	Wegener's granulomatosis	45 F	—	4	Coryza, hoarseness	Saddle nose	,,	+	−	+	−	−	−	+	Myocardial infarction
52	Bignami and Ficari (1956)	,, ,,	24 F	?1955	5	Earache	Purulent rhinitis	,,	−	−	+	+	−	−	−	
53	Morgan and O'Neil (1956)	,, ,,	26 M	1953	11	Gingivitis, neck ulcer	Loosening of teeth	,,	−	−	+	+	−	−	−	Myocardial infarction
54	Chatillon *et al.*, 3 (1956)	Wegener's angiitis	42 M	1955	6	Epistaxis, weight loss	Sinusitis	,,	+	−	+	+	−	−	+	Cardiac failure
55	Short, 1 (1957)	Stevens–Johnson syndrome	25 M	1949	1	Chest pain, cough	Nasal block, hoarseness	Cough, pain	+	−	+	−	−	−	+	
56	Rose and Spencer, 87 (1957)	Polyarteritis nodosa	49 M	1950	3	Fever, earache	Otorrhoea	Cough	−	+	−	−	+	−	+	Cardiac failure

Once signs of dissemination have occurred the general condition has always deteriorated and death has ensued from uraemia or secondary bronchopneumonia (Table I).

Clinical investigations of note are summarized in Table III. The radiological changes in the lungs are of particular interest. In just over half of the cases dense circular or oval opacities are present in one or more lobes (Fig. 1), often showing central cavitation, and varying in size up to that of a hen's egg. Less often bronchopneumonic infiltration is the only change of note.

TABLE II.—*Symptoms and Signs in 56 Cases of Wegener's Granulomatosis*

	No.	Per Cent.
Upper air passages	50	89·3
Rhinorrhoea and/or sinusitis	34	60·7
Nasal obstruction without rhinorrhoea	4	7·1
Epistaxis	18	32·1
Saddle nose	5	8·9
Gum pain or ulcer	7	12·5
Hoarseness	8	15·3
Dysphagia	3	5·4
Otorrhoea and/or deafness	18	32·1
Eyes	23	41·1
Conjunctivitis	17	30·4
Proptosis	5	8·9
Dimness of vision	3	5·4
Scleritis	6	10·7
Lungs	27	48·2
Cough	22	39·3
Haemoptysis	6	10·7
Pleural pain	11	19·6
Urinary tract	14	25·0
Oliguria	10	17·9
Haematuria	4	7·1
Skin rash	26	46·4
Polyarthritis	19	33·9
Peripheral neuritis	16	28·6

TABLE III.—*Clinical Investigations in 56 Cases of Wegener's Granulomatosis*

	No. of Cases Examined	Abnormal	
		No.	Percentage
Radiography:			
Skull: sinus opacities	21	18	85·7
Lung shadows	40	38	95·0
Round and discrete		23	57·5
Bronchopneumonic infiltration		10	25·0
Haematology:			
Microcytic anaemia	33	32	97·0
Leucocytosis	56	38	67·9
Eosinophil leucocytosis	37	17	45·9
Urine:			
Albumin	42	37	88·0
Erythrocytes	42	34	81·0
Leucocytes	42	21	50·0
Casts	42	28	66·7
Biochemistry:			
Uraemia	27	23	83·2
Hyperglobulinaemia	10	8	80·0
High blood pressure	33	8	24·2

No specific aetiological agent has been isolated in any case. From examination of sputum and nasal swabs in 24 cases, the only pathogens isolated were *Staphylococcus aureus* from 14, a haemolytic streptococcus from 7, *Streptococcus viridans* from 4, and pneumococci from 3. Culture for fungi was negative in five out of eight cases; in the others *Actinomyces bovis* (twice), *Candida albicans*, and a "leptothrix" were isolated. A positive blood culture, a positive blood Wassermann reaction, and isolation of tubercle bacilli have each been reported once, but otherwise these investigations have always been negative. Similarly, all agglutination tests have been negative.

Pathology

The most striking changes occur in the respiratory tract. Extensive ulceration, often widespread, with necrosis of underlying cartilage and bone, is present in the nose, paranasal sinuses, palate, pharynx, and/or glottis in about three-quarters of the cases (Table IV). Most also show multiple shallow ulcers in the trachea and bronchi. The lungs were abnormal in all but two cases (Nos. 20 and 50). Rounded nodular areas of consolidation, greyish white in colour, measuring up to 4 cm. in diameter, and sometimes showing central cavitation, are usually present in one or both organs. Less frequently pale miliary nodules scattered diffusely through all zones, or varying degrees of consolidation, are noted. Infarcts were described in Case 36 only.

TABLE IV.—*Sites of Respiratory Tract Ulceration in 56 Cases of Wegener's Granulomatosis*

	No.	Per Cent.
Nose and nasal sinuses	34	60·7
Mouth and pharynx	21	37·5
Tongue	7	12·5
Larynx	14	25·0
Trachea	17	31·5*
Bronchi	23	42·6*

* Per cent. of 54 cases.

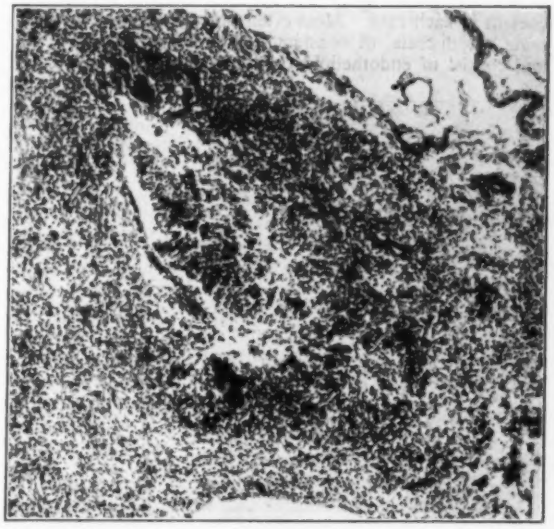

FIG. 2.—Case 3. Lung. (Haematoxylin and eosin. ×65.) A bronchiole showing intense granulomatous inflammation with early necrosis. Two giant cells of foreign-body type are present.

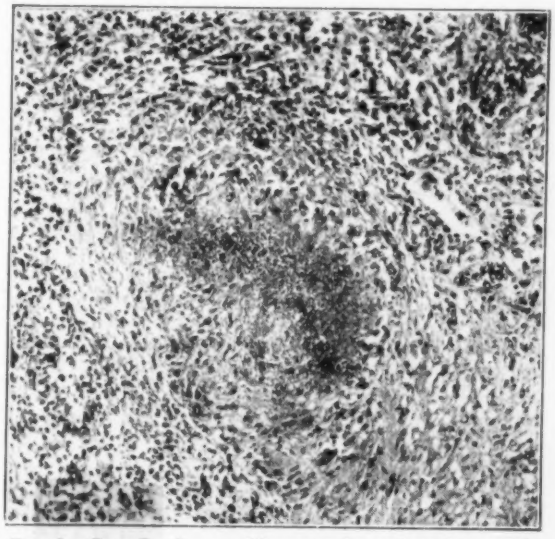

FIG. 3.—Case 7. Lung. (Haematoxylin and eosin. ×230.) Granuloma with numerous giant cells and extensive central necrosis.

Irrespective of their site, the lesions of the respiratory tract in my cases have a constant histological pattern (Fig. 2), that of granulomatous inflammation spreading deeply from the mucosa of the respiratory passages into the surrounding tissue. Intrapulmonary bronchial ulceration is especially common. Giant cells, of both Langhans and foreign-body type, are very numerous in the granulation tissue, and widespread necrosis often affects both cartilage and bone. Many of the pulmonary lesions are clearly peribronchiolar or prove so to be in serial section studies, and the rounded areas of consolidation visible macroscopically are seen to be conglomerate areas of peribronchial and peribronchiolar necrosis. Vessels near the lesions are implicated in the inflammation but show no features to suggest a specific vascular disease: thus the changes in these vessels are often confined to the segment next to the granulomatous focus. No micro-organisms can be demonstrated in appropriately stained sections of lesions in any of my cases.

In addition to the ulceration of the respiratory tract, widespread granulomata and foci of vascular necrosis are present in each case. Most often perivascular, the granulomata are discrete, of constant tuberculoid pattern (Fig. 3), and consist of endothelioid cells in radial arrangement and Langhans type giant cells with a sprinkling of lymphocytes, plasma cells, and both neutrophil and eosinophil polymorphonuclear leucocytes. Central necrosis of mature lesions is constant. The vascular lesions are focal, independent of the granulomata, and affect small arteries and arterioles, occasionally venules. The acute stages (Fig. 4) show "fibrinoid" necrosis of all layers, destruction of the muscle and elastica, mural thrombosis, and neutrophil infiltration. Healing lesions, present in most cases, show organization and recanalization of both the necrotic vessel wall and the luminal thrombus.

FIG. 4.—Case 4. Spleen. (Haematoxylin and eosin. ×90.) Pulp arteriole at a bifurcation. One limb shows acute "fibrinoid" necrosis and perivascular polymorph infiltration.

These widespread lesions, the incidence of which is given in Table V, are most frequent in lung, spleen, and kidney, though the number varies from case to case and organ to organ. Sometimes—for example, Cases 8 and 19—the granulomata are very numerous and visible as pale nodules about 0.1 cm. in diameter in many organs; in others the vascular lesions are very numerous, producing infarcts in kidney, spleen, heart, and testis.

The kidneys deserve special mention, having been severely affected in all but Cases 18, 30, and 45. Enlargement and blurring of the architecture are the usual macroscopic changes. Focal "fibrinoid" necrosis of glomerular loops and periglomerular granulomatous inflammation, often with giant cells, are almost constant histological findings. In my cases about a third of the glomeruli are usually affected, the inflammation and necrosis frequently involving the afferent or efferent arterioles.

Discussion

Despite the wide range of symptoms occurring in these cases, a constant clinical pattern is clear—that of a disease process beginning with symptoms and signs of an inflammatory lesion in the respiratory tract, continuing with evidence of widespread inflammation, and terminating in renal or respiratory failure. In most, especially Cases 4, 9, 10, 47, 48, and 49, the priority of the lesions of the respiratory tract is quite clear, and a definite time interval, of up to three years (Case 47), has often elapsed before the onset of widespread disease. In the early reports (Klinger, 1931; Rössle, 1933; Wegener, 1936, 1939) nasal lesions were prominent. Later authors (Postel and Laas, 1941; Weinberg, 1946; Ringertz, 1947; Johnsson, 1948; Godman and Churg, 1954), in describing cases in which tracheo-bronchial and pulmonary changes were more striking, noted their similarity to Wegener's cases. As each type shows similar local and widespread histological features, it is clear that they differ only in the level in the respiratory tract of the initial lesion. Furthermore, tracheo-bronchial or pulmonary lesions were present in all except Cases 20 and 50, and lesions in upper air passages may have been overlooked in some or all of the 12 cases in which such were not recorded.

TABLE V.—*Incidence of Disseminated Lesions in 54 Cases of Wegener's Granulomatosis*

	No.	Per Cent.
Discrete granulomata	54	100
Upper air passages	28	51·9
Trachea	10	18·5
Lungs	44	81·5
Spleen	30	55·6
Kidney	36	66·7
Liver	9	16·7
Lymph nodes	11	20·4
Heart	6	11·1
Prostate	4	7·4
Brain and meninges	4	7·4
Other organs	4	7·4
Focal necrotizing arteriolitis	54	100
Upper air passages	14	25·9
Lungs	47	87·0
Spleen	42	77·8
Kidney	42	77·8
Liver	10	18·5
Heart	15	27·8
Intestine	13	24·1
Skin	9	16·7
Adipose tissue	8	14·8
Voluntary muscle	8	14·8
Pancreas	5	9·3
Adrenal	6	11·1
Testis	5	9·3
Gall-bladder	4	7·4
Peripheral nerve	4	7·4

To date, including those of the present series, at least 56 cases which satisfy the diagnostic criteria of Godman and Churg (1954) have been reported, often as polyarteritis nodosa, malignant granuloma, or lethal midline granuloma. There can be little doubt, though, that the condition is more common than at first appears, as many cases have been excluded from the series only because of the absence of full data—namely, those of Siegmund (1936), Schürmann (1936), Moore *et al.* (1951), Rojas (1952), Geist and Mullen (Case 1, 1953), Breckenridge *et al.* (Case 3, 1954), Alexander (Case 3, 1954), Cutler (Case 2, 1955), Friedmann (Cases 4, 5, and 7, 1955), Paterson (Cases 1, 2, and 6, 1956), Rogers and Roberto (Cases 1 and 2, 1956), French and Civin (1956), Kelly (1956), McKibben and Bayliss (1956), Chatillon *et al.* (Cases 1 and 2, 1956), and Singh *et al.* (Cases 1 and 4, 1958), and others mentioned by Godman and Churg (1954). A further estimate of the frequency of the condition can be gained from the analysis of 104 cases of polyarteritis nodosa by Rose and Spencer (1957). Of these, one, Case 87, is a typical example of Wegener's granulomatosis, while four others, Cases 81, 82, 84, and 89, had granulomata of the upper respiratory tract and are almost certainly further examples.

Of the 56 cases, 33 have been male and 23 female. All age groups save the very young have been affected, the youngest patient being aged 12 years, the oldest 75, with the peak incidence in the fourth and fifth decades.

The pathological features of Wegener's granulomatosis were defined by Godman and Churg (1954). I believe, however, that the renal lesions are simply vascular and

granulomatous lesions as seen in other organs but modified by the local architecture. The basic pathological features of the syndrome are thus: first, giant-cell granulomatous ulceration at one or more levels in the respiratory tract; secondly, widespread giant-cell granulomata, discrete and frequent in lung, kidney, and spleen; thirdly, generalized necrotizing lesions of small vessels, again most common in lung, kidney, and spleen. The initial lesion is that in the respiratory tract, a granulomatous inflammation spreading from the mucosa, but there is little doubt that subsequent thrombosis of small vessels contributes to the development of the large necrotic areas in nares, glottis, and lung. The widespread granulomata resemble those found in experimental serum sickness (Rich, 1942), "allergic granulomatosis" (Churg and Strauss, 1951), and many cases of fatal drug sensitivity (Waugh, 1952; O'Brien and Storey, 1954; Rasmussen, 1955; and others). The necrotizing vascular lesions are morphologically similar to those in polyarteritis nodosa of the "microscopic" variety (Davson *et al.*, 1948), "hypersensitivity angiitis" (Zeek, 1952, 1953), and experimental hypersensitivity (Rich and Gregory, 1943; McKeown, 1947; Crawford and Nassim, 1951; Germuth *et al.*, 1955; and others).

As Fahey *et al.* (1954) have remarked, Wegener's granulomatosis closely resembles, both clinically and pathologically, several other uncommon diseases "which run in a spectrum from pure necrotizing and granulomatous processes without vasculitis through mixed forms to pure arteritis without granulomas." This close resemblance has led to many cases being described under a wide range of titles (Table I). Klinger (1931), Ringertz (1947), Ahlström *et al.* (1953), Rose and Spencer (1957), and others regarded their cases as variants of polyarteritis nodosa, whilst many authors have been impressed by the similarity of the local lesion in Wegener's granulomatosis with that in malignant granuloma of the nose (Woodburn and Harris, 1951; Geist and Mullen, 1953; Alexander, 1954; Friedmann, 1955; Paterson, 1956; Singh *et al.*, 1958). Furthermore, Fienberg (1955) was impressed by the similarity of his cases with Loeffler's syndrome and "allergic granulomatosis," and suggested that all three conditions be grouped as "pathergic granulomatosis." Yet neither in polyarteritis nodosa, malignant granuloma, Loeffler's syndrome, nor "allergic granulomatosis" is ulceration of the respiratory tract associated with widespread granulomata and vascular necrosis, and I agree with Godman and Churg (1954) in their comment, "The remarkable similarity of the pathological changes in all the cases . . . makes it probable that we are dealing with a peculiar and separate syndrome."

Early Course and Development

The early course in Wegener's granulomatosis is one shared by many diseases, ranging from tuberculosis to neoplasm. The diagnosis should be suspected whenever these can be excluded and destructive lesions in the respiratory tract persist despite antibiotic treatment. When evidence of widespread disease, such as haematuria, uraemia, polyarthritis, and peripheral neuritis, supervenes, the diagnosis is clear. Eosinophilia, conjunctivitis, the characteristic round shadows in chest radiographs, and a haemorrhagic skin rash are confirmatory features. The clinical diagnosis can be supported by biopsies from the ulcerative lesions, which are accessible in the upper air passages in three-quarters of the cases, and here eosinophilia, giant cells, and focal granulomata help in the differentiation from malignant granuloma. Biopsy of the skin lesions, which are micro-infarcts due to arteriolar thrombosis, is useful to demonstrate vascular necrosis. In patients in whom the initial or major lesion is in the lung, the obtaining of biopsy material by thoracotomy or bronchoscopy is justifiable in the early stages.

It is clear that two phases, sometimes merging but more often distinct, are involved in the development of Wegener's granulomatosis. The ulceration of the respiratory tract is primary, and the widespread lesions occur later in the natural history of the disease. As polyarteritis nodosa thus cannot be the primary disease, and as no specific micro-organism has yet been demonstrated, the aetiology is unknown. Most authors infer that an immunological reaction is involved. Fienberg (1953b) has suggested that the primary lesion is an Arthus phenomenon localized to the bronchial tree, and Kahn (1954, 1955) that the local ulceration is a reaction to an antigen circulating in the blood stream. Yet the evidence is incomplete and the aetiology of the primary lesion must still be regarded as uncertain.

In so far as the widespread, or secondary, lesions are concerned, there is considerable evidence that a hypersensitivity mechanism is involved. First, such a reaction is clearly the causal agent of similar or identical vascular and granulomatous lesions found in diseases such as scarlet fever (Hoyne and Steiner, 1940; Peale *et al.*, 1946) and other infections (Helpern and Trubek, 1933; Contratto, 1947; Bohrod, 1948), asthma (Wilson and Alexander, 1945; Teilum, 1946; Churg and Strauss, 1951), allergic dermatitis (Miale *et al.*, 1947; Rytand *et al.*, 1948), and serum sickness (Clark and Kaplan, 1937; Rich, 1942), in drug reactions (see above), or produced experimentally by measures designed to induce hypersensitivity in animals (see above). Secondly, many of the features of the terminal illness, such as the purpuric skin rash and stomatitis, migratory arthritis, eosinophilia, and transient pareses, are well known to occur in hypersensitivity states (Rich, 1946–7). Thirdly, the raised serum globulin level suggests an antibody response. Finally, impressive evidence came from Case 4, in which symptoms and signs of widespread disease appeared only during and after hypersensitivity reactions to streptomycin (Leggat and Walton, 1956). Widespread lesions morphologically similar to those in the other cases were found at necropsy, but were absent from a lung biopsy made before streptomycin therapy had begun. It is therefore probable that the secondary lesions in Wegener's granulomatosis are due to a hypersensitivity reaction, a drug (Cases 4, 5, 37, and 38) or tissue breakdown products being possible antigens.

Treatment

Many forms of empirical therapy have been unsuccessful. The temporary improvement that sometimes follows antibiotic treatment is probably due to control of secondary infection. Steroids occasionally produce remission (Case 45; Moore *et al.*, 1951; Cutler, 1955), but are more often ineffectual (Cases 39 and 52; Alexander, 1954; Bandler and Campbell, 1954; Paterson, 1956). I believe that the treatment of choice is radiotherapy to the local lesion, with control of secondary infection by suitable antibiotics, and that steroids should if possible be withheld until the local lesion has healed, owing to the danger of hindering the defence against infection of the open respiratory lesions.

Many cases of healing of malignant granuloma of the nose following *x* rays in low dosage have been reported, and it is logical to try this method on the very similar local lesion in Wegener's granulomatosis. The palatal and nasal lesions in my Cases 9 and 10 were thus healed, and Seidelin and Willcox (1954) and Singh *et al.* (1958) also report success with radiotherapy.

Steroids are the treatment of choice for the widespread lesions once the ulceration of the respiratory tract is healed. They reduce the antibody response (Bjørneboe *et al.*, 1951), inhibit the development of vascular lesions in sensitized animals (Rich *et al.*, 1950; Seifter *et al.*, 1950; Germuth and Ottinger, 1950; and others) and appear to induce healing of the vascular lesions in polyarteritis nodosa (Baggenstoss *et al.*, 1951; Symmers and Litchfield, 1952). The signs of widespread inflammation in Case 9 disappeared following cortisone therapy, the nasal and laryngeal lesions already having been healed by radiotherapy, and the patient has remained well for nearly two years. Cortisone also produced remission of symptoms in Case 10.

Conclusions

The constant clinical course and the presence in all cases of standard anatomical features suggest that the condition under discussion is a separate entity, even though it is closely linked, both morphologically and pathogenetically, with malignant granuloma, periarteritis nodosa, and other granulomatous and vascular diseases. Though the first cases recorded were those of Klinger (1931) and Rössle (1933), it was Wegener (1936, 1939) who first described the disease in detail, and it has come to be known as Wegener's granulomatosis. Including my 10 cases, at least 56 are on record, but many others, less well documented, are probable further examples of the disease.

The natural history clearly has two phases. Beginning with symptoms of chronic nasal or pulmonary infection, it continues with evidence of widespread inflammation. Though a few cases have lived for up to four years, in the majority death rapidly ensues from renal or respiratory failure, the average course being about five months. The clinical diagnosis, though difficult in the early stages, can be confidently made whenever to an ulcerative lesion in the respiratory tract is added evidence of widespread inflammatory disease. The radiological changes in the lungs are typical, and eosinophilia and biopsy of the local lesion or of skin are of confirmatory value.

The diagnostic pathological features are granulomatous ulceration at any level in the respiratory tract and widespread giant-cell granulomata and necrotizing lesions of small vessels. The characteristic round or oval consolidations in the lungs are not infarcts but conglomerate areas of peribronchial necrosis. The severe and constant changes in the renal corpuscles are focal, do not represent diffuse glomerulonephritis, but are simply granulomatous and vascular lesions modified by the local architecture.

The initial lesion in Wegener's granulomatosis is not polyarteritis nodosa, but the ulceration in the respiratory tract, the aetiology of which is uncertain. The widespread lesions occur later in the course of the disease and there is impressive evidence that they are the result of a hypersensitivity reaction. Treatment should be primarily directed towards healing of the initial lesion, and radiotherapy has proved successful in some cases. Administration of cortisone or other steroids is the treatment of choice once widespread lesions have occurred.

Summary

Wegener's granulomatosis is an uncommon syndrome in which giant-cell granulomata in the respiratory tract occur together with granulomatous and vascular lesions resembling those in polyarteritis nodosa. In this work, which is based on a study of 10 cases, and 46 others selected from the literature, the clinical and pathological features are described and tabulated.

The disease is clearly a separate entity, differing both clinically and in the character and distribution of the lesions from similar conditions, such as polyarteritis nodosa and malignant granuloma. It begins as a progressive ulceration of unknown aetiology in the respiratory tract. Sooner or later widespread lesions, the result of a hypersensitivity reaction, complete the disease picture. Treatment of the lesions of the respiratory tract by radiotherapy has been successful in a few cases.

ADDENDUM.—Since this paper was written, I have seen further reports of cases of Wegener's granulomatosis by Fanger and Hoffman (1957), Plummer *et al.* (1957), Levine and Madden (1957), Read and Treip (1957), Stoeckle *et al.* (1957), and Gordon *et al.* (1957).

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THE HUMAN FACTOR AS A CAUSE OF DELAY IN DIAGNOSIS IN GENERAL PRACTICE

BY

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This article is a record of delays in the diagnosis of major organic disease by a general practitioner during the two years 1956 and 1957.

As minor delays of diagnosis, in the strictest sense, occur from day to day, the following criteria have been adopted and all cases filling them have been included. (1) The case must be one of serious organic disease, which was for a time thought to be a minor or neurotic illness, or some illness not allied to the true condition. (2) The delay in diagnosis must be actually or potentially dangerous to the patient. (3) The practitioner must feel in retrospect that he might have diagnosed the case earlier, and feel worried on that account; this may seem a strange criterion, but in actual fact it is very important, as any practitioner who is reasonably conscientious and honest with himself will know if he might have made an earlier diagnosis with the evidence available.

The third criterion would not, therefore, include a patient with carcinoma of the lung who is sent for *x*-ray examination only when his cough becomes persistent; a patient complaining of abdominal pain who on observation develops signs of appendicitis, which at operation proves to be an "early appendix"; a patient who is sent to hospital for diagnosis, and the diagnosis is determined by special investigations.

It is difficult to assess cases in retrospect, and great pains have been taken to be as fair and frank as possible by trying to avoid distortions of memory and by referring carefully to notes made about the patient at the time. This is not an attempt to excuse delays of diagnosis, but to assess the factors that led to the delay. I have long formed the impression that many delays of this sort are due not only to the intrinsic difficulties of the diagnosis but also to a "human factor" which for some reason has obscured the issue. The following cases are recorded to determine if that impression is true.

Case 1

This patient was admitted to hospital with a compound fracture of the tibia and fibula. While in hospital he had considerable difficulty with his bowels, and in spite of the administration of purgatives his constipation was troublesome. When he returned home his practitioner visited him once a week in order to inquire after his leg, which was in plaster, and give him his certificate. During this time he complained of troublesome diarrhoea, which did not respond to treatment with mist. kaolin. et morph. or, later, to a course of succinylsulphathiazole. It was only on the sixth visit that careful questioning showed that he was actually suffering from tenesmus and faecal incontinence, and a rectal examination revealed a carcinoma of the recturn. This proved to be inoperable, and a palliative colostomy was performed.

It is quite clear that the correct diagnosis would have been made earlier if the patient had not fractured his leg. The practitioner and the hospital staff were concerned with the leg, and the bowel symptoms were regarded as an awkward side issue, and hence did not receive sufficient attention.

Case 2

The practitioner was called to see the patient's wife when she had a stroke. As he was leaving the house the patient said, "As you are here, Doctor, would you mind giving me something for my sore lip?" Somewhat irritated, the practitioner reopened his case, and filled in a prescription for penicillin cream, after glancing at the patient's lip to confirm that there was a sore place.

Four months later the patient came to the surgery with an unconnected complaint, and an indurated ulcer of the lip was noted. This proved to be an epithelioma, which fortunately responded well to treatment.

In this case the practitioner was concerned with a major illness of the wife, and the intrusion of the apparently minor illness of the husband, in rather irritating circumstances, prevented a diagnosis from being made.

Case 3

This patient was in the third month of pregnancy when she began to experience anorexia and nausea, and after 48 hours she sent for her doctor. On questioning she admitted to frequency of micturition, constipation, and a slight ache in the right side of the abdomen, in addition to the above-mentioned symptoms. Examination revealed rather diffuse tenderness under the right costal margin and in the right loin. She was pyrexial, with a temperature of 101° F. (38.3° C.), and her tongue was furred. The urine showed a trace of albumin, but was not sent for microscopy.

A diagnosis of pyelitis of pregnancy was made, but when, after 48 hours' treatment with sulphonamides and mist. pot. cit., the expected improvement did not take place, a specimen of urine was sent for microscopy, which revealed the absence of leucocytes. A consultant gynaecologist was therefore asked to see the patient, and she was admitted to hospital with a tentative diagnosis of appendicitis. Her symptoms remained unchanged, and after a further period of 48 hours laparotomy was performed. During the exploration a retrocaecal appendix abscess ruptured, and the abdomen was closed with a drain inserted. The patient made a rapid recovery and was delivered at term with no complications.

In this case no human factor was involved.

Case 4

A woman of 87 resided in a nursing-home and was visited about every six weeks by her practitioner. Five months before her death she had a syncopal attack with a transient weakness of the left leg, which was thought to be due to cerebral thrombosis. Her blood pressure was 90/60 mm. Hg.

On the day before her death she collapsed and had a convulsion. On examination shortly after this she was found to be unconscious, with signs of acute congestion of the lungs. It was also realized that she was a typical case of myxoedema, and had had the following signs and symptoms: mental slowness, susceptibility to cold (she always wore a shawl), scanty hair, croaking voice, baggy eyes, slow pulse, and low blood pressure. The matron, who had known the patient for a long time, said that she had been like that for many years, during which time she had been seen by several doctors.

The delayed diagnosis was of academic interest, as she was a dying woman, and death was thought to be caused by cardiac failure due to myxoedematous myocarditis.

In this case the patient was often visited, and as she was an old person the visits tended to be more of a social than a medical occasion. The diagnosis should have been made at the first visit; once the practitioner had become used to the appearance and eccentricities of the patient the diagnosis became difficult. It cannot, however, be said that the human factor was of major importance, and this was really a "classical" error. It is unlikely that the myxoedema shortened her life to a great extent, but with suitable treatment her last years would have been spent in closer contact with reality.

Case 5

In this case a diagnosis of carcinoma of the lung was missed in a hypochondriac. The patient, a man aged 68, was a long-established hypochondriac to the extent of being a byword in the practice. Since the death of his wife, three years previously, he had complained of pains in various parts of the body, and had spent long periods in bed. On one occasion a consultant surgeon was asked to see him at home during an attack of severe abdominal pain, and agreed with the diagnosis. During the last nine months of his life the pains occurred mostly in the chest. He was being visited at monthly intervals, and his chest was examined frequently but no abnormality was discovered. Finally the neighbours who looked after him felt that they could no longer manage, and a consultant geriatrician was asked to see him with a view to admission to a long-stay hospital. On examination the consultant made a diagnosis of carcinoma of the lung, with solidification of the left apex and deviation of the trachea.

This patient was seen so often that the gradual change of the pain "from the general to the particular" went unnoticed, as also did the gradual decline in health. The chest was often examined, but always with the expectation of finding nothing, and hence the localized signs at the apex were never elicited. There is a strong human factor in this case, as after many visits the practitioner developed an attitude of mind whereby he too readily assumed that the symptoms were hypochondriacal.

Case 6

A girl student, who was not on the practitioner's list but was living as a lodger with the practitioner's family, was noticed one day to be walking with a limp, and, when asked about it, said that she had strained her groin while climbing a hill three weeks before and had had some treatment from her own doctor.

The matter was forgotten, and the slight limp soon ceased to be noticed. Two months later she said one morning that she had been kept awake by pain in her groin. She was examined and a mass of lymph nodes was found in the groin; also a depressed circular scar was noted in front of the tibia, where a histologically benign melanoma had been excised one year previously. The diagnosis of metastasizing melanoma was unfortunately confirmed, and a block dissection was carried out by a consultant surgeon, but it was not possible to remove the growth entirely. The patient died six months later.

In this case the patient was living in such close contact with the practitioner and his family that the slight limp was ignored. If she had been the practitioner's patient and had come to see him at the surgery the diagnosis would probably have been made earlier, but the tragedy would not have been averted.

Case 7

This case is primarily one in which a diagnosis of acute appendicitis was delayed in an obese patient. However, the human factor was of some importance, although it is rather difficult to portray adequately in a short description.

The patient, a medical auxiliary by profession, telephoned the doctor to say that he had suffered from pains in the abdomen for 24 hours. He asked if the doctor could visit him at about 1 o'clock, as he had appointments to see clients until then. The practitioner complied with this request.

On questioning, the patient said that he had had abdominal pain with anorexia, but no vomiting or disturbed bowel action. On examination no tenderness was elicited, except for some slight tenderness in the right groin near the scrotum. The practitioner understood the patient to say that he had taken his temperature and that it was normal; afterwards the patient said that it had been raised, so there must have been some misunderstanding on this point.

The patient had recently been under treatment for renal colic, and the practitioner felt that the pain was probably of renal origin, although a definite diagnosis was not made. He instructed the patient to telephone if the pain became worse or if the temperature went up, and arranged to visit next morning.

On calling next morning the practitioner found that the patient's pain had been worse, although, out of good nature, he had not telephoned. He was still at work. On examination there was some diffuse tenderness in the right iliac fossa, and the temperature was 100.6° F. (38.1° C.). He was sent to hospital with a diagnosis of ? acute appendicitis, ? genito-urinary disease.

At operation a gangrenous disintegrating appendix was discovered. The patient recovered well, but has unfortunately developed a small discharging fistula, for which further operative treatment is under consideration.

In this case it is unfortunate that there were several factors which helped to delay the diagnosis: the obesity of the abdomen; the recent history of renal colic; the fact that the patient was a medical auxiliary, which led the practitioner to put too much responsibility on the patient in that he did not take the temperature himself, and that he told the patient to telephone instead of making another visit himself in the evening. There was also a subtle factor in that the patient tended to play down his symptoms, and the very nature of the telephone call tended to lull the practitioner's suspicions. When the practitioner's partner was told about the case he said: "He is just the sort of person one would miss a diagnosis on." This was very true, although the human factor was not the major one.

Case 8

In this case the condition concerned was one of pregnancy, and, although this is not a major organic disease, it is a major organic condition, and the delay in diagnosis might have had serious consequences, particularly so far as the baby was concerned.

The patient was a very neurotic person who attended the surgery fairly often with symptoms for which there was rarely any organic basis. Three years previously she had given birth to a baby which had died three weeks after delivery.

On this occasion she was the last patient in the evening surgery. Her complaint was that of "bubbling in the stomach." Although this sounded a symptom which was unlikely to indicate organic disease, the practitioner examined the abdomen, and was surprised to find a definite enlargement of which the patient had been unaware. The abdominal muscles were so tense that he was unable to determine the nature of the enlargement. Vaginal examination was also surprisingly difficult, as the perineal muscles were so tense that he was unable to palpate the cervix, but was able to determine that there was a large mass attached to the uterus. The patient was vague when asked about her periods, but appeared to have had irregular bleeding. A search for foetal heart sounds, using an ordinary, not a foetal, stethoscope, was unsuccessful.

The practitioner, who was suffering from considerable fatigue at the time, was confused by the whole matter and referred the patient to a specialist. In retrospect it might have been wiser to have seen the patient again and searched for the foetal heart with a foetal stethoscope, or to have arranged for an *x*-ray examination of the abdomen.

However, fate stepped in (as the reader may have anticipated) and two nights later the practitioner's partner and the midwife were faced with the delivery of the baby without any preparation. The baby weighed 5 lb. (2.5 kg.), and was probably about four weeks premature.

There is no doubt that the patient, following the loss of her first baby, subconsciously repressed her knowledge of the second pregnancy to such an extent as to deceive herself and prevent her doctor from making a definite diagnosis. She therefore received no antenatal treatment, and this, with the history of the previous confinement, might have been disastrous.

This may seem an incredible case, but it is stressed that a thorough examination was carried out. Although the practitioner's course of action was probably affected by fatigue, it is considered there was no major human factor in this case, as is explained later.

Case 9

A man aged 77 came to the surgery complaining of a sore mouth. He was edentulous, and on the gum of the left lower jaw at the back of the mouth there was an area of exudate. He wore dentures, and had not had a new set for 15 years. It was felt that this was a traumatic lesion due to rubbing of the dentures, and he was told not to wear them and to see his dentist with a view to obtaining a new set. He was also given a simple mouth-wash.

At his next visit he said that the pain had almost gone, although the area of exudate was still present. About three months later he returned and said that his mouth still troubled him and was sometimes painful. On examination it was obvious that there was an ulcer present, although this was still partly concealed by exudate. The surgeon to whom the patient was sent wrote: "I agree with you that the ulcer is almost certainly malignant. It has rather rolled everted edges and seems to be involved in the mandible." A biopsy showed it to be a squamous-cell carcinoma, and deep *x*-ray therapy was begun.

The delay in the diagnosis was due to the fact that the practitioner came to the conclusion that the ill-fitting denture was the cause of the trouble, and, when improvement took place, did not follow the case closely. Also the case was in the borderline between medicine and dentistry, and was receiving treatment from both sources. The most important factor was that the practitioner had not seen a similar case before.

Case 10

This patient, an 84-year-old man, was deaf. He wore a hearing-aid that scarcely contributed to his hearing, for it was so noisy that the practitioner, while sitting in his surgery, could hear the squeaks and whistles from it while the patient was in the waiting-room. The usual procedure was for the patient to place a note on the doctor's desk, with some request written on it, as, for example, "Can I have some black medicine for a cough?" He was in fact a quaint and lovable character.

On three occasions in a period of four months the note read, "Can I have some medicine for diarrhoea?" On the third occasion the practitioner's suspicions were aroused, and he arranged to examine the patient at home. The rectum was full of faeces, but, following an enema, a high rectal tumour was palpated.

On questioning the relatives it became clear that the patient had had bowel symptoms for many months. The human factor is obvious, and in fact this case was included only after some thought, as, although there had been a dangerous delay, the practitioner felt that he had not done too badly.

At operation the consultant surgeon was able to perform an end-to-end anastomosis, and the prognosis is considered good.

Observations

This series is far too small to be of any statistical significance, but the following observations may be made on the 10 cases described. (1) The human factor played a major part in the delay of diagnosis in five cases (Nos. 1, 2, 5, 6, and 10) and a minor part in two (Nos. 4 and 7). (2) Six of the patients suffered from malignant diseases. This large proportion is due largely to the criteria of selection, but it does stress how insidious malignant conditions may be, especially in old people. Four of these six patients were over 65. (3) Four cases (Nos. 1, 3, 4, and 10) may be described as classical errors—that is, errors against which one is warned in standard textbooks. (4) Two cases (Nos. 5 and 8) could be described as neurotic. This is a surprisingly small proportion, as from my own experience and that of my colleagues it appears to be a fairly common cause of the masking of a diagnosis. (5) It was hoped to make observations on the effect on the prognosis of the delay in diagnosis, but this has been difficult. In all malignant cases any delay will make the prognosis worse, but after studying the cases in great detail it is felt that the only one in which the ultimate prognosis may have been greatly affected was Case 9.

The Human Factor

The human factor may be defined as an attitude of mind of the doctor towards the patient, which influences his judgment in such a way as to make it more difficult for him to come to a correct diagnosis. This factor may be due to the particular circumstances of the interview or to an attitude of mind which has developed over many past interviews.

In the first type the doctor may be in a frame of mind where his judgment is clouded owing to fatigue, boredom, ill-health, worry, or because he is in too much of a hurry; or he may be irritated by the patient or the circumstances of the visit.

In the second type the doctor's judgment may be blunted in one of several ways. He may see the patient so often that the visit becomes social rather than medical; he may know the patient to be neurotic or a hypochondriac, and anticipate that all his symptoms are of this type; he may be treating the patient for one particular disease, and discard irrelevant symptoms without adequate consideration. Also he may know the patient socially to such an extent that he is unwilling to examine the patient thoroughly—for example, to carry out a rectal or vaginal examination. It is well known that if a doctor treats persons he knows very well—for example, a member of his family—he often treats them badly.

It is stressed that the mere fact that the patient is neurotic does not imply that a human factor is operating, but only if the patient's neurosis has built up an attitude in the doctor's mind.

These facts are, no doubt, well known to all doctors of experience, but it is felt that this article may be useful as a reminder to them, and as a warning to others entering practice. A medical student, in particular, is led to believe that the really serious error is, for example, to call a diastolic murmur systolic; time will show him how relatively unimportant this sort of mistake is. In general practice serious organic disease forms a small part of the daily work, and it is in the mass of vague, trivial, and neurotic complaints that the human factor thrives.

In hospital practice the human factor is of far less importance. Most cases are regarded as serious organic disease until proved otherwise and receive a full examination by at least one doctor, and probably routine investigations as well. It is not the task of the consultant to decide if the patient should be fully examined, whereas it is a decision which the general practitioner must make in every case; and that is one of the chief difficulties of his work. He is more likely to miss a diagnosis through failing to examine a case than through performing an examination and missing a physical sign. To make this clear it must be understood that at every surgery a general practitioner may expect to see several patients with vague complaints, particularly of "feeling tired" or "needing a tonic." These symptoms are usually due to mild depression or anxiety, but any of them may be due to serious organic disease, which requires urgent diagnosis and treatment. The practitioner has not the time to examine and investigate them all, and indeed if he had it would be a soul-destroying task. He must pick and choose, and his selection is bound to be affected by non-medical factors, in particular by the number of patients waiting to see him and by whether the patient presents the history intelligently or stupidly.

This article is concerned with the work of one particular general practitioner, of particular temperament and methods

of working. But it is felt that the experience of other practitioners may be similar.

To guard against the intrusion of the human factor the doctor must first of all know himself and know his weaknesses. Secondly, he must enjoy his work, and have adequate spare time and leisure. Thirdly, he must not have a larger list than he is capable of dealing with. Fourthly, he must organize the practice for his own and his patients' benefit, even if this means making rules which may seem petty and tiresome to the patients themselves. In short, he must have an efficient mental discipline; and herein the fundamental difficulty of general practice lies. If his mental discipline is too rigid he is bound to lose some personal contact with his patients; if his personal contact is too strong, on the other hand, he cannot exert efficient mental discipline. A book could be written on the subject.

Summary

A record has been made of delays of diagnosis, following stated criteria, over a period of two years. Observations are made on these cases. In 5 out of 10 cases a human factor was thought to have played a major part in the delay. This factor is defined and discussed.

I wish to thank my partner, Dr. J. F. Mitchell, and Dr. T. A. Richards for their help and encouragement, and all those consultants of the Northampton General Hospital to whom most of the cases mentioned finally came for treatment and advice.

INFECTED CORK CLOSURES AND THE APPARENT SURVIVAL OF ORGANISMS IN ANTISEPTIC SOLUTIONS

BY

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The dangers of infected cork closures have been repeatedly emphasized since the original description by Lowbury (1951). Antiseptic solutions are thought to be contaminated by contact with the cork during shaking and by being poured through the infected neck of the bottle. Since the organisms are frequently killed by the antiseptic when exposed *in vitro*, it has always seemed that such contamination must needs be intermittent, and that when the container is left undisturbed the contents should be sterile. A specimen of cetrimide sent to these laboratories for examination showed such persistent and repeated contamination, even when left undisturbed, that it gave support to the original comment that "organisms were growing in the solution." It was therefore decided to investigate the mechanisms of contamination which might lead to the apparent survival of organisms in an otherwise lethal fluid.

Examination of Infected Cetrimide Solution

The specimen consisted of half a gallon (2.2 litres) of 1% aqueous cetrimide contained in a glass flagon and sealed with a bark cork 1½ in. (4 cm.) in diameter. On arrival at the laboratory the fluid level was below the bottle neck, which was dry. The cork was also dry, fissured but otherwise intact. 0.1 ml. of the solution was placed in 100 ml. of nutrient broth and incubated for 18 hours. A segment of the cork, excised with a sterile scalpel, was cultured in a similar fashion. Both specimens yielded a heavy growth of a motile Gram-negative rod with the biochemical reactions of a paracolon bacillus. A pour-plate made at this time showed approximately 760 organisms per ml. of cetrimide solution. The container was left undisturbed at room temperature for seven days and the plate count was repeated. Samples were taken by removing the cork and passing a sterile pipette into the solution. Care was taken not to touch the neck of the bottle or the cork. The count on this occasion was 57×10^2 viable organisms per ml.

Experiment 1. Sensitivity of Infecting Organism to Cetrimide in Vitro.—Preliminary tests, using the tube titration method and pour-plates incorporating varying concentrations of fresh cetrimide, showed that the organism was consistently inhibited by a dilution of 1:1,000 cetrimide. The bactericidal concentration was determined by adding 1-ml. quantities of an overnight broth culture to 9 ml. of varying concentrations of aqueous cetrimide. After five minutes' exposure the inoculum was centrifuged down, washed twice with saline to remove residual cetrimide, and either placed in 100 ml. of nutrient broth or diluted for viable counting. With this technique, 1:1,000 cetrimide appeared bactericidal, in all but one of the experiments, for inocula of the order of $11,000 \times 10^{16}$ viable organisms per ml. The method used was more exacting than the random loop sample employed by Calman and Murray (1956), and this accounts for the greater concentration necessary to achieve a bactericidal effect in aqueous solution. The contaminating organism was none the less rapidly killed when exposed *in vitro* to one-tenth of the original concentration of cetrimide.

Experiment 2. To Exclude Growth Factors in Cetrimide Derived from Cork.—In view of the experimental findings of Nelson (1942), the cetrimide solution was examined for the presence of growth factors which might allow either survival or multiplication of contaminants. A portion of the solution was Seitz-filtered to remove organisms and examined by two-dimensional chromatography, using as solvent 80% alcohol and phenol saturated with water. The sample, which failed to reduce Benedict's solution, showed no hexoses, pentoses, or amino-acids. A cork extract, prepared by autoclaving 5 g. of cork in 100 ml. of distilled water, was similarly negative.

Experiment 3. To Exclude Physical Protection of Organisms by Cork Extracts.—10 ml. of the cork extract prepared in Experiment 2 was incorporated in 100 ml. of 1% aqueous cetrimide. This solution was used to repeat the sensitivity tests performed in Experiment 1. No protection of the inoculum could be demonstrated under these conditions, and the bactericidal figure remained unchanged. These findings agree with the experiments of Lowbury (1951), who concluded that his infected solutions contained insufficient solutes to protect added organisms.

Experiment 4. Self-sterilizing Properties of Contaminated Cetrimide Solutions.—Since the paracolon bacillus was rapidly killed by cetrimide *in vitro*, it was decided to investigate the behaviour of the contaminated solution after removal from its original container. 10 ml. of the contaminated cetrimide was carefully removed and transferred to a sterile screw-capped bottle. A time-clock was started and an immediate viable count performed (20 seconds elapsed between removal of the cork and the second tenfold dilution). The count showed 950×10^2 viable organisms per ml. Exactly five minutes after the transfer, volumes of 0.1 and 0.5 of the cetrimide were incorporated in pour-plates, and further samples were diluted for viable counting. No organisms were detected in these volumes of solution. This experiment was repeated on a number of occasions with identical results. It was therefore concluded that contaminated solutions of cetrimide are self-sterilizing within a short time of removal from their original container. Since, in this experiment, the solution had not come into contact with either the cork or

the bottle neck, it was thought that the physical act of removing the cork must in some way contaminate the solution at the moment of sampling.

Experiment 5. To Demonstrate the Mechanism of Contamination on Removing the Cork.—The neck of the flask was cut off with an emery wheel, leaving the handle intact (see Fig.). The infected cork was removed and the glass sterilized by steaming. The apparatus was then held over an exposed agar plate, and the contaminated cork inserted and removed once. Inspection of the surface of the agar with a plate microscope showed countless particles of cork dust adhering to the surface. Subsequent incubation revealed numerous colonies of the infecting organism. The shape and size of these colonies suggested that they had arisen from particles infected with numerous organisms rather than from single cells. The experiment was therefore repeated, holding the apparatus over 1 ml. of nutrient broth in a sterile container. This was shaken to disperse the organisms and a viable count performed. The contaminated broth contained 50×10^2 viable organisms per ml.

Experiment 6. Contamination of Other Antiseptic Solutions with Infected Cork.—The cork from the original flask was inserted, in turn, into flasks containing 10% aqueous dettol (new formula), 1:1,000 aqueous benzalkonium chloride ("zephiran"), and 1:2,000 aqueous chlorhexidine ("hibitane"). Paracolon bacilli could be readily recovered from all the solutions after one or two insertions of the infected cork. All solutions showed the same self-sterilizing properties as the original cetrimide when removed to another container.

Experiment 7. Histology of Infected Cork Closures.—A segment of the cork was excised and embedded in paraffin. Sections approximately 6 μ in thickness were cut and stained by Gram's method. The main cellular structure of the cork was seen to be free of organisms. In certain parts of the section, however, the normal pattern was replaced by necrotic areas containing dark amorphous debris. In these fields large masses of Gram-negative bacilli could be seen, many lying free at the edge of the section. These areas seemed to represent the blackened fissures seen in many cork closures.

Discussion

The mechanism of contamination outlined above offers an explanation for the otherwise puzzling phenomenon of organisms recoverable from a bactericidal solution at any given moment of sampling. Although each manipulation of the infected cork releases a shower of infected cork dust on to the surface of the liquid, the actual numbers of organisms recovered will be inversely proportional to the time elapsing between removal of the cork and transfer of the sample to media which dilutes it beyond its bactericidal concentration. It is interesting to note that the viable count performed in Experiment 4, which was done in the shortest possible time after sampling, yielded the highest number of organisms recorded throughout this series of experiments.

In the routine culturing of such a contaminated solution, the sampling time is remarkably short and was found not to exceed 15 seconds in a number of experiments, even when manipulating a graduated pipette. It is therefore scarcely surprising that positive cultures can be obtained repeatedly from solutions that have been contaminated in this way. Such results may give the impression that organisms are surviving in the antiseptic, and wide variations in the count due to different sampling times may even suggest that multiplication is taking place. Dust from infected corks can contaminate a variety of antiseptic solutions, and the phenomenon does not appear to be confined to cetrimide. Histology of the cork suggests that organisms colonize the fissures in large numbers, and that dry, friable closures are particularly likely to produce infection in this manner. Although the experiments of Nelson (1942) demonstrate that cork extracts can allow the multiplication of coliform organisms in distilled water, the nutrients concerned do not appear in solutions with cork closures in sufficient concentration to be detected by chromatography. Contaminating organisms, however, can clearly multiply in the interstices of corks, since it is scarcely credible that the large numbers seen in sections could have arisen from direct implantation only.

The self-sterilizing effect demonstrated in these experiments cannot excuse the continued widespread use of cork closures in bottles of all types containing solutions which may come into contact with an open wound. In addition to the mechanism described, contamination of a solution also occurs by direct contact with the cork or bottle neck, and only a few seconds may elapse between pouring the solution into a receiver and transferring it to the patient's skin.

Summary

A series of experiments which were carried out to investigate the apparent survival of a contaminating organism in an antiseptic solution are summarized.

A method of contamination is described which accounts for positive cultures obtained at any given moment of sampling. The apparent persistence of contaminants in a lethal solution is thereby explained.

The experimental contamination of other antiseptic solutions is demonstrated, and the dangers of cork closures are once again emphasized.

We are indebted to Miss Margaret Coles for chromatographic analysis of the solutions, to Mr. Martin Hansen for the histological sections, and to Mr. W. Nolan for the photograph. Our thanks are also due to Mr. Darwin, of I.C.I., for generous supplies of cetrimide and "hibitane" during this investigation.

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Young Children in Hospital, by James Robertson (Tavistock Publications, Ltd., 4s. 6d. net), is a book reviewing the problem of the young child in hospital separated from his mother. It is based on a memorandum submitted on behalf of the Tavistock Clinic and the Tavistock Institute of Human Relations to the Committee on the Welfare of Children in Hospital appointed by the Central Health Services Council. It embodies experience the author obtained in the joint Child Development Research Unit of the Tavistock Clinic and Institute. Mr. Robertson has also made a documentary film, *Going to Hospital with Mother*, complementing the book. It describes how a mother of a young child can help when her child is admitted to hospital for an operation. The film is 16 mm. and runs for 45 minutes. It is available (hiring fee 25s.) from the Tavistock Institute of Human Relations, 2, Beaumont Street, London, W.1.

Billy Goes to Hospital is a "comic" intended for children about to enter hospital and is issued by the Department of Child Health, Guy's Hospital. Also from Guy's is a leaflet for the parents of such children, of which the cost of printing has been met by the hospital's Guild of Ex-patients and Friends. Its purpose is to help parents prepare children for this experience and so prevent consequent emotional upset.

SOME PHYSIOLOGICAL RESPONSES OF NEONATAL ARTERIAL BLOOD PRESSURE AND PULSE RATE

BY

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AND

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To assess the extent to which the neonatal vascular system is capable of responding under physiological conditions, the influence of alterations in posture and of crying on the arterial blood pressure and pulse rate was observed during the first twelve days of life.

Material and Methods

A study was made of 71 normal infants ranging from 3 hours to 12 days old. The birth weight ranged from 4 lb. 1 oz. to 9 lb. 10 oz. (1,840 g. to 4,365 g.), only two falling into the premature-weight group. All had been born by spontaneous delivery and none had been distressed. The measurements were made in the afternoon one-half to two hours after a feed; the infants were awake but quiet.

Blood-pressure measurements were made on all the infants and repeated observations on 28 of these during their first 12 days of life. The pulse rate was counted in 14 of the babies, repeated observations being made on seven of these.

The systolic blood pressure was measured by palpation as described previously (Holland and Young, 1956). The pulse rate was counted from E.C.G. records taken continuously over three two-minute periods. The record was obtained from a precordial lead and one arm; the electrodes were held in place by "selotape." The average of three blood-pressure and pulse-rate readings taken with the child lying supine were recorded.

The effect of posture was then determined, both in the "feet-down" and in the "head-down" position, by tilting the cot at an angle of 80 degrees; the child needed supporting by the shoulders during these procedures. During these manœuvres the position of the arm in which the blood pressure was measured was kept at approximately the same level in relation to the heart and the mercury manometer. The first arterial blood-pressure measurement was made within 30 seconds of the change in posture and was followed by two more readings within two minutes. Finally, the blood pressure was measured when the infant was crying in the supine position.

On six occasions the intrathoracic pressure was recorded in quiet and in crying babies in the supine position; this was measured by a Hansen capacitance manometer from a water-filled fine "polythene" tube introduced into the oesophagus (Dornhorst and Leathart, 1952).

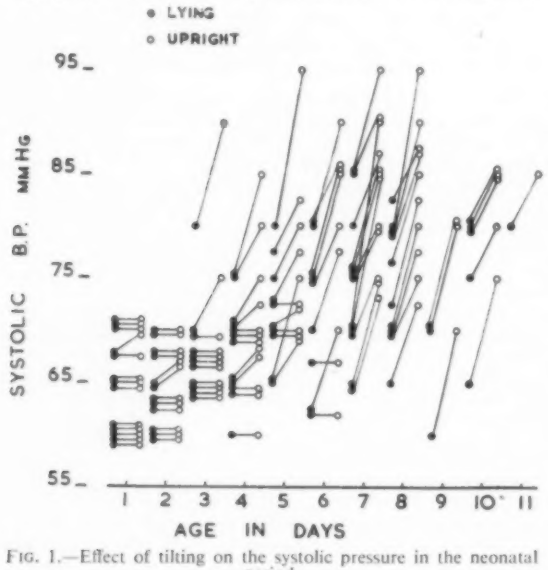

FIG. 1.—Effect of tilting on the systolic pressure in the neonatal period.

Results

Arterial Blood Pressure.—Fig. 1 shows that tilting into the feet-down position did not alter the systolic pressure during the first three days of life in 31 out of 36 infants; between four and six days after birth a rise was observed in 20 out of 31 infants, and in all the older infants there was a rise in systolic pressure in response to tilting. The rise did not exceed 12 mm. Hg. Tilting into the head-down position did not alter the systolic pressure in any of the infants studied at any age. Fig. 2 shows that the pattern of the response, with respect to the age of the infant, was the same for crying; the blood-pressure changes were greater, and often a rise of 20 mm. Hg was observed.

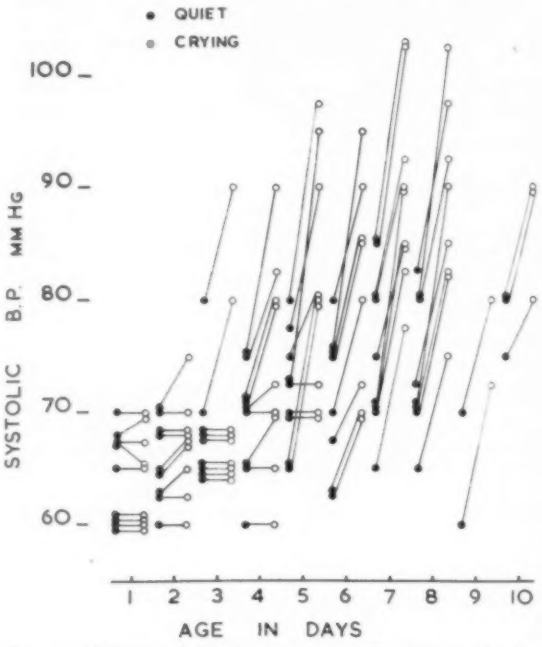

FIG. 2.—Influence of crying on the systolic pressure in the neonatal period.

Pulse Rate.—Fig. 3 shows that in 37 out of 50 observations the heart rate rose varying amounts from a few beats to 40 beats a minute in response to tilting into the feet-down position; one-half of these showed an increase of 15–20 beats a minute. The variation in response was evenly distributed throughout the period studied, as were the occasions on which there was no acceleration of the heart rate. Crying regularly caused an increase in pulse rate of about 40 a minute. Inspection of Fig. 3 shows that the resting pulse rate increased during the first 10 days of life in the group of infants studied. To substantiate this rise the resting pulse rate was measured in a further group of 12 infants, each on at least three days during this early neonatal period; the results are shown in Fig. 4.

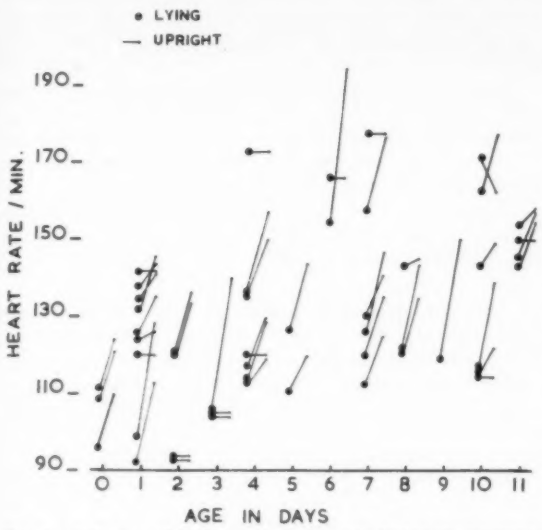

FIG. 3.—Influence of tilting on the heart rate during the neonatal period.

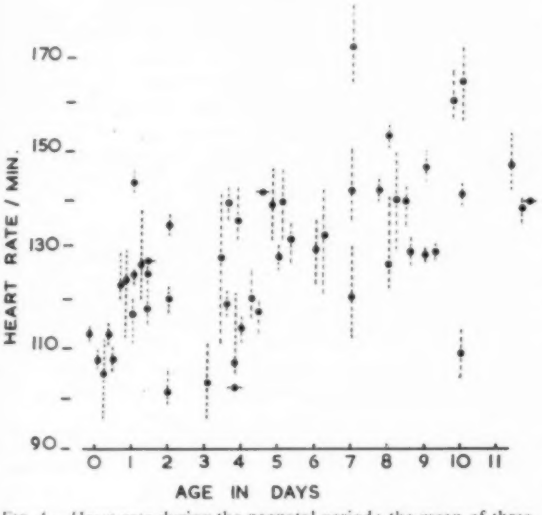

FIG. 4.—Heart rate during the neonatal period; the mean of three readings is shown, together with the lowest and the highest limit.

Discussion

The increase of heart rate of about 35 a minute which occurs during the first 10 days of life accompanies the small rise in resting systolic pressure which was observed during this time. Vierordt (1906) recorded no change in pulse rate during a similar period.

Effect of Posture on the Neonatal Blood Pressure

In the normal adult a passive change of posture from the supine to the feet-down position causes an immediate fall in mean arterial pressure; recovery is rapid, and after about 30 seconds the mean pressure returns approximately to the recumbent level, with a decrease in pulse pressure and an acceleration of the heart rate. These changes have been observed both by Wald, Guernsey, and Scott (1937), using a "tycos" self-recording sphygmomanometer, and by Brigden, Howarth, and Sharpey-Schafer (1950) during continuous recording of intra-arterial pressure with a condenser manometer. The present observations on the newborn infant were made at a time corresponding to the recovery period in the adult, and have two special features: firstly, during the first four days of life there was no change in systolic pressure on tilting into the feet-down position; and, secondly, during the succeeding 10 days there was always a small rise of systolic pressure after tilting. There was usually an acceleration of the heart rate in response to tilting in both age groups.

As these findings in the infant are, at present, isolated from other circulatory data during tilting, any consideration of them can only be speculative. The neonatal circulation may differ from the adult in several respects. Firstly, the venous pressure: during the first 24 hours of life this is relatively high, +3 to +5 cm. H_2O in the supine position (Mollison and Cutbush, 1949; Bonham-Carter, Bound, and Smellie, 1956), and until it is adjusted to adult levels may influence the arterial blood-pressure response to tipping. It might be expected that hydrostatic effects due to tilting would be smaller in the infant than the adult and that the reduction in venous pressure would be proportionately less; further, the relatively large head of the infant is enclosed in a non-rigid box and will contain a greater proportion of the total blood volume than in the adult, and on account of this it is possible that the equilibrium pressure of the venous column will be higher in the upright than in the supine position. The available data (Bonham-Carter *et al.*, 1956) show that the fall in the venous pressure in response to tilting during the first 24 hours of life is of the same order as that found in the adult (Brigden *et al.*, 1950); nevertheless, the venous pressure of the infant in the upright position is higher than in the tilted adult.

The second difference between the newborn and adult circulation is likely to be the degree of vasomotor activity. The maintenance of the systolic pressure at the recumbent level after tipping during the first few days of life suggests activity of the baroreceptors, though the acceleration of the heart rate accompanying the rise of arterial pressure in the older infants is not typical of a baroreceptor response and may be from the venous side.

Thirdly, the course of the circulation in the newborn infant may also influence blood-pressure responses; Adams and Lind (1957) have shown that the ductus arteriosus may be open and that there may be a reversed flow of blood through it, for pulmonary hypertension may persist in the normal infant for two weeks after birth.

Effect of Crying on the Neonatal Blood Pressure

Since the pattern of the response is the same with respect to the age of the infant both for crying and for tilting, it is tempting to suggest: (1) common mechanisms for the responses, and (2) that there is some fundamental change in the circulation occurring four to five days after birth. However, the situation is complicated by the large pressure changes occurring in the chest during crying, which may change rapidly from a negative to a positive sign, as such transients are known to be transmitted to the arterial system. Little is known of sympathetic activity during stress in the infant, and indeed such activity may also account for the blood-pressure responses to tilting.

Summary

The response of the systolic blood pressure and of the pulse rate to tilting into the feet-down position and to crying has been studied during the first 12 days of life.

During the first three to five days of life neither tilting nor crying altered the systolic blood pressure.

In the subsequent week of life both tilting and crying caused a rise in systolic pressure; the response to the latter was the greater.

The pulse rate increased in response to tilting.

The possible mechanisms which may be concerned are discussed, and it is suggested that there is some fundamental change in the neonatal circulation four to five days after birth.

Tilting into the head-down position did not alter the systolic pressure during the first 12 days of life.

We thank Dr. J. Forest Smith and Mr. A. J. Wrigley for allowing us to make these observations on their cases; Sisters Gale and Harris and the midwives for their kind help and co-operation; Professor Henry Barcroft for facilities; and Dr. A. C. Dornhorst for valuable comments.

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INTRINSIC FACTOR AND VITAMIN B_{12} ABSORPTION*

BY

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With the isolation of vitamin B_{12} (cyanocobalamin) it soon became obvious that Castle's original hypothesis was erroneous and that intrinsic factor did not react with an extrinsic factor to form haematinic principle which was stored in the liver. The more simple concept was formed that intrinsic factor was concerned with the absorption of vitamin B_{12} from the intestine. This led to much intensification of work connected with its isolation and possible clinical application.

Glass, Boyd, Rubinstein, and Svigals (1952) demonstrated that it was associated with a more or less crude mucoprotein fraction of the gastric juice, and they therefore suggested that it might also be mucoprotein in nature. In my own laboratory, work was carried out on the preparative paper strip electrophoresis of human gastric juice (Latner, Ungley, Cox, McEvoy-Bowe, and Raine, 1953). A substance with intrinsic factor activity was present on the anode section of the paper strip. It contained hexosamine and was therefore probably mucoprotein in nature. This led to further chemical procedures and the eventual preparation of highly potent material.

The first work which we carried out was concerned with precipitation at low *p*H and subsequently with alcohol at low temperatures (Latner, Merrills, and Raine, 1954). We soon realized that this could possibly lead to breakdown of biological material, and we therefore decided to attempt isolation of the factor by the use of ion-exchange resins. This led to the production of a highly potent product which had a molecular weight of approximately 15,000 (Latner, Merrills, and Raine, 1956). The material was homogeneous on electrophoresis at two different *p*H values, as well as in the ultracentrifuge. Its activity, both clinically and by the radioactive vitamin-B_{12}-absorption test, was higher than any material previously described. There was little doubt that the material was a mucoprotein.

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Williams, Ellenbogen, and Esposito (1954) have prepared a substance of molecular weight 5,000 which also had high intrinsic factor activity. Since they used trypsinization in their isolation procedure it was not unlikely that they might have broken down a substance of higher molecular weight. An important point, however, was the fact that both their material and our own possessed very low vitamin-B_{12}-binding power.

Holdsworth (1957) has claimed to have isolated a substance of molecular weight 40,000 which has vitamin-B_{12}-binding power and which is highly active as intrinsic factor.

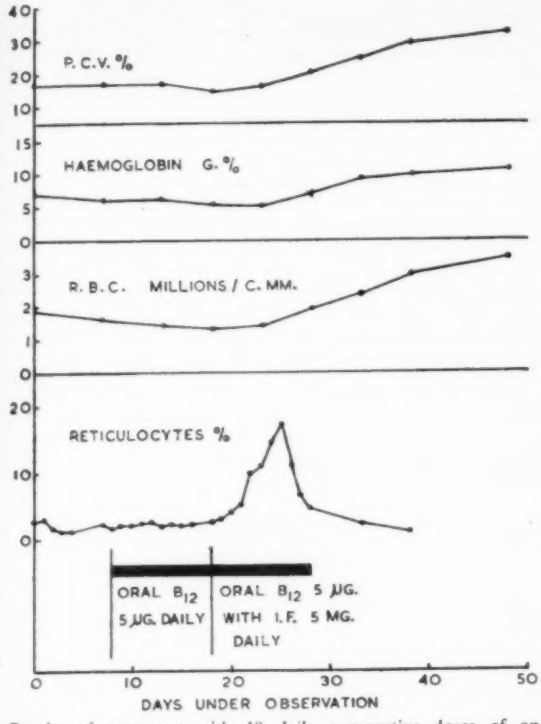
It seems that three substances with intrinsic factor activity have been prepared from pig gastric mucosa—a mucopolypeptide with a molecular weight of 5,000, and two mucoproteins, one with a molecular weight of approximately 15,000 and another with molecular weight of 40,000. This has led to some confusion. If one considers Holdsworth's material as a possible precursor of intrinsic factor produced by the gastric mucosa and that modification of this precursor both in the stomach and in the small intestine eventually leads to intrinsic factor of relatively low molecular weight, then the whole position is more or less clarified. In relation to this concept it is interesting to note that O'Brien, Taylor, Turnbull, and Witts (1955) have prepared from human gastric mucosa a substance with intrinsic factor activity which has a molecular weight of about 40,000. Its activity in human beings was much less than the pig material we ourselves have isolated. It seems, therefore, that the material in question should really be regarded as a precursor of intrinsic factor.

Absorption Tests

In order to try to shed some light on this rather confusing picture, we have for some time been undertaking isolation procedures with freeze-dried pig pyloric mucosa. After treatment by ion-exchange and precipitation procedures this has yielded a preparation which has proved remarkably potent on clinical trial (see Fig.). There is no doubt that the clinical response was completely maximal. We gave 5 mg. of our intrinsic factor preparation daily together with 5 μg. of vitamin B_{12}. We have therefore carried out intestinal absorption tests at this dosage, and we have been able to demonstrate that we were able to bring about an absorption of approximately 2 μg. daily.

It is interesting that the ion-exchange procedures have also led to the isolation of material which has proved to be inhibitory to vitamin-B_{12} absorption (Latner and Merrills, 1957). This material is mucoprotein in nature, possesses a molecular weight approximately equal to that of the intrinsic factor mucoprotein, but has a different tyrosine : tryptophan ratio. The behaviour on electrophoresis is remarkably like that of the intrinsic factor. The existence of such a substance is of the highest significance. Recent work throwing possible doubt on the efficacy of prolonged oral treatment in pernicious anaemia (Schwartz, Lous, and Meulengracht, 1957) should not be regarded as the final word in this matter. It is obviously still necessary to test preparations which are known not to contain inhibitor. Especially is this the case since the inhibitory effect in rats is still present some weeks after a single dose of inhibitor has been taken (Latner, unpublished observations).

We will now consider the physiological mechanisms concerned with the absorption of vitamin B_{12} and the


P. C.V. %
HAEMOGLOBIN G. %
R. B. C. MILLIONS / C. MM.
RETICULOCYTES %
ORAL B_{12} 5 µG. DAILY
ORAL B_{12} 5 µG. WITH I.F. 5 MG. DAILY
DAYS UNDER OBSERVATION

Results of treatment with 10 daily consecutive doses of an intrinsic-factor preparation and vitamin B_{12} compared with a control period with vitamin B_{12} alone.

part played by intrinsic factor. A good deal of experimental work in this field has recently been carried out on rats. This is because their absorption mechanism has proved to be similar to that in human beings (Clayton, Latner, and Schofield, 1955; Watson and Florey, 1955).

Control of Intrinsic Factor Production

Nervous.—A number of normal human beings apparently absorb very little vitamin B_{12} under the conditions of the usual radioactive vitamin-B_{12}-absorption tests. If these individuals are given an injection of carbachol (0.25 mg.) at the same time as they are given their radioactive vitamin B_{12} there is an increase in absorption (Baker and Mollin, 1955). This would appear to indicate that parasympathetic stimulation increases the production of intrinsic factor, since carbachol has no effect on absorption in patients with pernicious anaemia.

Endocrine.—Bacon Chow (1956) has shown that after hypophysectomy in rats there is markedly diminished absorption of vitamin B_{12}. This is due to diminished production of T.S.H. Thyroidectomized animals behave in a similar fashion. We have shown that antithyroid drugs inhibit the absorption of the vitamin in the rat (Clayton and Latner, unpublished observations). It would seem, therefore, that the endocrine system plays some part in the absorption mechanism, but that the details of this action are still to be worked out. The effect might be on production of intrinsic factor or directly on the intestine itself.

Site of Absorption of Vitamin B_{12}

Evidence is accumulating with regard to the actual site of absorption of vitamin B_{12}. Our own work with the rat has indicated that most of the absorption occurs in the middle third of the small intestine (Latner and Raine, 1957a). This has been confirmed (Booth, Chanarin, Anderson, and Mollin, 1957). It is interesting that the vitamin is first of all taken up by the intestinal wall and not released from this situation for approximately one hour. Cooke, Cox, Meynell, and Gaddie (1957) have come to the conclusion that in human beings absorption occurs mainly in the lower ileum. This has been deduced from studies of vitamin-B_{12} absorption in patients with ileitis.

Mechanism of Absorption of Vitamin B_{12}

Some light is at last being shed on the possible mechanism of absorption of vitamin B_{12}. There is some controversy on whether or not binding of the vitamin by intrinsic factor is important in this respect. This, of course, arises from the fact that our own and Williams's intrinsic factor preparations bind very little vitamin B_{12} but are very potent, whereas other preparations have definite vitamin-B_{12}-binding power. Much work has recently been published which indicates that binding of the vitamin is important. It is, however, a matter of some significance to point out that, although binding has been demonstrated to be of some consequence, it is not necessarily binding to intrinsic factor itself, but may well be to another constituent of the concentrate under investigation. It would be difficult, however, to adopt this point of view in the case of a vitamin-B_{12}/intrinsic-factor complex (Holdsworth, 1957) which appears homogeneous by various physical methods of examination. However, it is possible that even in this material we really have intrinsic factor forming a complex with another protein which itself has high binding power for the vitamin.

Using the urinary excretion test of absorption of the vitamin, Schilling and Schloesser (1957) performed some interesting experiments which demonstrate the importance of binding. Normal human gastric juice was incubated with radioactive vitamin B_{12} and then the normal vitamin was added. Another sample of the juice was incubated with ordinary vitamin B_{12} and then the radioactive vitamin added. In this way two portions of gastric juice were prepared which contained equal total quantities of the vitamin, but one sample possessed the radioactive vitamin in the bound form and the second the non-radioactive vitamin in this state. Each sample in turn was fed to patients. Evidence was gained from the excretion of radioactivity in the urine that there was preferential absorption in the bound form. Similar observations have recently been made in Castle's laboratory using gastrectomized rats as experimental animals (Nieweg, Shen, and Castle, 1957).

A number of workers have shown that pig intrinsic factor concentrates inhibit absorption of vitamin B_{12} in the intestine of the intact rat. Similar findings with some intrinsic factor preparations have been observed in healthy human beings, but other preparations increase absorption (Williams, Chow, Ellenbogen, and Okuda, 1957). It has been suggested that this inhibition phenomenon may be some form of species specificity of intrinsic factor, but it now seems likely that it is due to the presence of some inhibitory substance. Possibly vitamin-B_{12} binding by inhibitory substances renders the vitamin unavailable to the animal in question. This idea is further supported by the fact that human gastric juice in doses of 0.5 ml. inhibits absorption in the rat, but much smaller doses increase absorption (Latner, unpublished observations).

Wijmenga (1957) has presented what I consider to be the most likely hypothesis in relation to the mechanism of vitamin-B_{12} absorption. He has suggested that this might take place in two stages. First, a special type of binding to some protein or proteins, and, secondly, the absorption of this bound form across the intestine under the influence of intrinsic factor.

Schilling and Schloesser (1957) have demonstrated that the binding of vitamin B_{12} by human gastric juice is highly specific with most samples. They have shown that adding large quantities of pseudovitamin B_{12} to gastric juice has no effect on the final binding power of the gastric juice for the vitamin B_{12}. They have also shown that administration of large amounts of pseudovitamin B_{12} has no effect on the

absorption of vitamin B_{12} itself in the human intestine, and so there is no form of competition for absorption between these two substances. They therefore suggest that a highly specific form of binding is important from the point of view of absorption and consider that this binding is to intrinsic factor itself, since the intrinsic factor preparation they used showed the same binding specificity. I would like to suggest that experiments of this type do not preclude a specific system in the gastric juice for binding vitamin B_{12} to some protein, in accordance with Wijmenga's suggested first stage. Eventually this specifically bound form is absorbed in the intestine under the action of intrinsic factor. Such a protein system could well have been present in the intrinsic factor preparation that Schilling employed. As I have already pointed out, our own material does not bind much vitamin B_{12}. We have evidence that to some extent this binding is inhibited by pseudovitamin B_{12}.

In my own laboratory, absorption has also been studied in the intact rat (Latner and Raine, 1957b). We have shown that pseudovitamin B_{12} does not compete for absorption with vitamin B_{12}, a finding which confirms the work of Schilling in the human. On the other hand, in our experiments with isolated rat intestine (Latner and Raine, 1958) we have demonstrated that there are two systems for vitamin-B_{12} uptake, one of which is competitive with pseudovitamin B_{12} and the other highly specific. It thus appears that the specific binding system of the intestine is concerned with the actual absorption of the vitamin, since this is unaffected by the pseudovitamin.

We have extended our vitamin-B_{12} uptake studies to liver slices (Latner and Raine, 1957c). Here we have demonstrated that the uptake is highly specific and is non-competitive with pseudovitamin B_{12}. The recent interesting observation (Miller, Raney, and Hunter, 1957) that intrinsic factor increases the uptake of the vitamin by liver slices has been confirmed. We have shown that this increased uptake is prevented by the addition of pseudovitamin B_{12}. It would thus seem at first sight that the increased uptake is part of a competitive system. We have, however, also determined by ultrafiltration the amount of vitamin B_{12} that is bound by the intrinsic factor preparation we used under various experimental conditions and shown that the liver uptake is in actual fact proportional to the amount of vitamin bound by the preparation. Pseudovitamin B_{12} inhibits the increased uptake because it inhibits binding. We are hoping that liver slices may be more simple to study than isolated intestine, since in isolated intestine there may well be some rat intrinsic factor which has been absorbed before the animal was killed. It is not impossible, therefore, that studies of liver slices which have not previously been in contact with intrinsic factor may possibly shed some light on the mechanism whereby the vitamin is absorbed into cells and possibly across the intestine. This is not too improbable a suggestion, since we must remember that embryologically the liver is formed by a budding-off process from the foregut.

We are also accumulating evidence that the absorption mechanism would appear to be enzymatic. In the first place, by giving increasing doses of radioactive vitamin B_{12} to the intact rat we have obtained an absorption curve of a type corresponding to the well-known Michaelis and Menton equation of enzyme activity in relation to substrate concentration (Clayton, Latner, and Schofield, 1957). Secondly, our vitamin-B_{12} analogue studies have demonstrated that the intestinal absorption is highly specific and is prevented by interchanging the desdimethyl moiety of vitamin B_{12} for adenine as in pseudovitamin B_{12}, or by altering one of the side chains on ring B of the vitamin (Latner and Raine, 1957a). This is a type of chemical specificity which is all too familiar in known enzyme mechanisms.

Action of Sorbitol

Recently it has been shown that sorbitol, a hexahydric alcohol derived from glucose, will increase the absorption of vitamin B_{12} from the intestine (Greenberg *et al.*, 1957). This arose from observations that the preparation "liptril" increased the absorption of vitamin B_{12} in healthy young and old people (Chow, Horonick, and Okuda, 1956). It has now been demonstrated that the component responsible for this effect is sorbitol. We have confirmed that this compound increases vitamin-B_{12} absorption from the intestine of the normal rat (Latner and Raine, unpublished observations). This, however, happens only when the dose of the vitamin, as well as that of the sorbitol, is very high and definitely outside physiological levels. The mechanisms involved are probably related to simple diffusion.

After sorbitol administration at high-dosage level there is great distension of the intestines, and we feel that this also plays some part in the increased absorption. It is highly debatable, therefore, whether the sorbitol effect is going to shed any direct light on the action of intrinsic factor itself, although it is a tempting notion that the carbohydrate moiety of intrinsic factor mucoprotein might be responsible for the absorption of vitamin B_{12}. Among various other substances tested (Greenberg *et al.*, 1957) it has been shown that D-mannitol, L-sorbose, and D-xylose also have the ability to enhance vitamin-B_{12} absorption.

Clinical Application

Diagnostic

The use of radioactive vitamin B_{12} in the study of intestinal absorption of the vitamin has naturally led to diagnostic applications. Absorption tests are of great value in patients who have been given vitamin B_{12} in spite of the fact that the diagnosis of pernicious anaemia was not definitely established before therapy was instituted. Help is also obtained in the differential diagnosis of subacute combined degeneration (Berlyne, Liversedge, and Emery, 1957). Studies are made before and after administration of an intrinsic factor preparation by mouth, and it is demonstrated that the intrinsic factor restores absorption to normal. Some normal people have a relatively low absorption, which can be increased by the administration of carbachol (Baker and Mollin, 1955), but no such increase occurs in patients with pernicious anaemia or subacute combined degeneration. The intestinal absorption of vitamin B_{12} is often defective in steatorrhoea, but in this instance intrinsic factor preparations produce no improvement.

The actual techniques of determining absorption involve giving a known dose of radioactive vitamin B_{12} by mouth and determining the amount that appears in the faeces (Heinle, Welch, Scharf, Meacham, and Prusoff, 1952; Callender, Turnbull, and Wakisaka, 1954) or in the urine (Schilling, 1953). In the latter instance it is necessary to give a massive flushing dose of ordinary vitamin B_{12} intramuscularly about an hour after the radioactive vitamin has been administered orally.

Other techniques have been elaborated which do not require the collection of either urine or faeces. They are the determination of intestinal absorption by measurement of radioactivity over the liver some days after administration of the test dose (Glass, Boyd, Gellin, and Stephanson, 1954), and, more recently, the study of the radioactivity of the blood, which rises to a maximum in normal individuals some eight hours after oral administration but does not rise in patients with pernicious anaemia unless an intrinsic-factor preparation is also given (Booth and Mollin, 1957).

Therapeutic

As has already been mentioned, it is still possible that intrinsic-factor preparations not containing inhibitor substances will play some part in the treatment of pernicious anaemia. Recent observations relating to diminished activity after prolonged administration must be repeated with non-inhibitory intrinsic-factor preparations before prolonged oral therapy is said to be contraindicated in pernicious anaemia. Unfortunately, insufficient material of this nature has so far been prepared for clinical trial.

It is now recognized, as a result of absorption studies, that there is defective vitamin-B_{12} absorption after total gastrectomy and in many instances after partial gastrectomy. It is therefore important that the vitamin should be administered intramuscularly to certain patients after these operations have been performed. Similar remarks apply to patients with ulcerative colitis and certain types of ileitis.

In view of the fact that large oral doses of vitamin B_{12} lead to appropriate absorption in the absence of intrinsic factor it is probably sufficient to administer massive dosage of the vitamin by mouth. This could apply to the treatment of pernicious anaemia, but remains to be proved by prolonged clinical trials. In any case, it is important to realize that patients who have developed megaloblastic anaemia as a result of defective absorption will have severe depletion of their vitamin-B_{12} stores. It is impossible to restore this to normal by intestinal absorption alone, and it is therefore important, in the first place, to give vitamin B_{12} in relatively large doses intramuscularly.

Summary

There are now at least three highly purified preparations of intrinsic factor, with molecular weights of approximately 5,000, 15,000, and 40,000 respectively. They are apparently homogeneous and belong to the group of mucoproteins. The two with lower molecular weights have low vitamin-B_{12}-binding activity.

A substance has also been obtained which inhibits vitamin-B_{12} absorption. The presence of such a substance or substances in intrinsic factor concentrates could explain certain inhibitory phenomena previously ascribed to species specificity. This has been borne out by the observation that human gastric juice in small quantities stimulates absorption of vitamin B_{12} in the rat but is inhibitory in larger amounts. The last word has not yet been said in relation to the clinical use of intrinsic factor preparations by mouth, since a single dose of the inhibitory substance maintains its effect on vitamin-B_{12} absorption for a long period.

Intrinsic-factor secretion is under the influence of the parasympathetic nervous system and possibly also the thyroid.

The intestinal absorption of vitamin B_{12} has been shown to occur in the middle third of the small intestine in the rat but possibly in the lower ileum in human beings.

It seems that some form of binding to protein is necessary for intestinal absorption of vitamin B_{12}. This binding need not be to intrinsic factor itself. Studies of absorption with increasing dosage, as well as with analogues of the vitamin, present evidence that an enzyme mechanism is involved in its intestinal absorption.

It has recently been shown that sorbitol, a hexahydric alcohol derived from glucose, increases the absorption of vitamin B_{12} from the intestine.

New knowledge in relation to intrinsic factor and vitamin B_{12} has proved of use both in diagnosis and in therapy, especially in relation to treated pernicious anaemia, subacute combined degeneration, gastric resections, and intestinal disorders.

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WEBER–CHRISTIAN DISEASE WITH VISCERAL INVOLVEMENT

AN EXAMPLE WITH HEPATIC ENLARGEMENT

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Although commonly known in English-speaking countries as Weber–Christian disease, a typical example of the syndrome was first published by Pfeifer (1892), and details of a second patient were described by Gilchrist and Ketron (1916). It was Brill (1936) who first referred to the condition as Weber–Christian disease, and on the Continent it is commonly known as Pfeifer–Weber–Christian disease. Weber (1925) drew attention to these two previously recorded patients in his own paper, and there is no doubt that to him must go the credit of recognizing the condition as a distinct entity. To Weber's original title "Relapsing Non-Suppurative Nodular Panniculitis" Christian (1928) added the word "febrile" to emphasize an important feature likely to arouse the interest of the clinician.

The object of recording this case in some detail is to emphasize that the disease has been too long considered as localized to the skin, whereas certain viscera and other organs may be extensively involved by the fatty metamorphosis. Such involvement may give rise to varied symptoms, including retrosternal pain, pain and swelling in joints, pain in bone, and also abdominal pain, and these symptoms may prove puzzling if the syndrome is not recognized. Rarely the visceral involvement is so extensive that it results in death.

The following case presented certain unusual features. There was severe fatty change in the liver, confirmed at laparotomy, and the only other example of such extensive hepatic involvement that we can find is that of Hanrahan *et al.* (1951). Unlike their case, which was fatal, our patient's hepatomegaly preceded the appearance of the typical skin lesions. Continuous pyrexia also preceded the rash by eleven weeks, thus rendering clinical diagnosis impossible in the early stages.

Case Report

A 63-year-old housewife was admitted to hospital on June 21, 1957, for investigation of persistent fever and malaise, which had been present throughout the previous three weeks. She had a history of rheumatic fever when she was 14, 20, and 21 years old, and had since become breathless on exertion. She married at 30 and had since borne three children with normal confinements. At the age of 62 she had a sudden onset of palpitation with dyspnoea, followed one week later by pleuritic pain due to a pulmonary embolus. On examination at that time she was found to have rheumatic heart disease with mitral stenosis and auricular fibrillation, but the liver was impalpable.

Her present illness began on June 1, 1957, with shivering, tiredness, and pyrexia. Prior to admission to hospital she had had persistent fever with an evening temperature of 99–101° F. (37.2–37.8° C.). On admission she looked and felt well, although she had signs of mitral stenosis with auricular fibrillation. The liver was enlarged 8 cm. below the right costal margin, had a smooth surface, and was easily palpable bimanually. The spleen could not be felt. There were no signs of heart failure and there was no anaemia, icterus, palmar erythema, spider naevi, or clubbing.

Investigations.—Liver-function tests: serum albumin, 4.45 g./100 ml.; serum globulin, 4.35 g./100 ml.; electrophoresis indicated an increase in gamma-globulin; serum cholesterol, 184 mg./100 ml.; thymol turbidity, 5 units; thymol flocculation, ++; serum bilirubin, 0.3 mg./100 ml.; alkaline phosphatase, 6.8 units. Her persistent pyrexia was investigated by blood culture, which was negative on five occasions; six catheter specimens of urine were examined with negative results; the Paul–Bunnell test was negative; a cholecystogram and intravenous pyelogram were both normal; her haemoglobin was 13.6 g./100 ml., W.B.C. 6,600 per c.mm., and the erythrocyte sedimentation rate (Wintrobe) 40 mm. in the first hour. Her electrocardiogram confirmed the auricular fibrillation and showed some depression of the ST segment over the left ventricle.

The fever continued in varying degree, once reaching 104° F. (40° C.), and it was occasionally 103° F. (39.4° C.), but usually between 99 and 101° F. (37.2 and 37.8° C.), often reaching normal for some period during the day. It was accompanied by moderate tachycardia. On one occasion (July 16) she developed a transient swelling of the right knee with a small effusion and limitation of movement. Further investigation of the hepatic function during this time showed some deterioration (serum albumin 4 g./100 ml., globulin 3.1 g./100 ml., thymol turbidity 9 units, thymol flocculation +++). She also gradually became anaemic (haemoglobin 8.9 g./100 ml.) without obvious cause, and laparotomy was considered justified in order to determine the exact nature of the hepatic enlargement. Two pints (1,140 ml.) of blood was transfused prior to the laparotomy by Mr. A. J. Heriot on July 26.

At operation the liver was found to be diffusely enlarged, pale in colour, and faintly mottled; the surface was smooth. The spleen was normal on palpation. A wedge of liver was taken for histological examination. Microscopically it showed the normal liver architecture to be maintained, but there was a moderate degree of fatty degeneration. There was no necrosis, fibrosis, or cellular infiltrate (Fig. 1). Following laparotomy the patient was apyrexial for three days but then developed further fever, which persisted for nine days, with a temperature rising to 104° F. (40° C.). One week later, on August 15, there appeared a firm, very tender subcutaneous nodule on the medial side of the right shin, with overlying erythema. The nodule measured 7 by 6 cm., and the overlying skin was lightly attached to it. The following day a similar but smaller nodule appeared on the left buttock, measuring 3 by 3 cm. The erythema gradually faded; there was faint mottling over the nodule on the leg for two days but no residual pigmentation or scarring. Both nodules gradually became less tender. On August 15, 15 days after its appearance, the nodule on the left buttock was excised. Section (Fig. 2) showed the epidermis and dermis to be normal, but the subcutaneous fat included in the section showed changes throughout. These consisted of varying-sized foci of reticulo-endothelial cells lying between the fat cells. These macrophages had a foamy cytoplasm and some were multinucleate. In some areas there were small collections of polymorphonuclear leucocytes and, here and there, considerable numbers of eosinophils. There was no necrosis or fibrosis. The subcutaneous arteries showed a severe degree of obliterative endarteritis.

A second transfusion of 2 pints (1,140 ml.) of blood corrected the hypochromic anaemia. The patient was discharged from hospital on September 17, and has since remained well. There has been neither further panniculitis

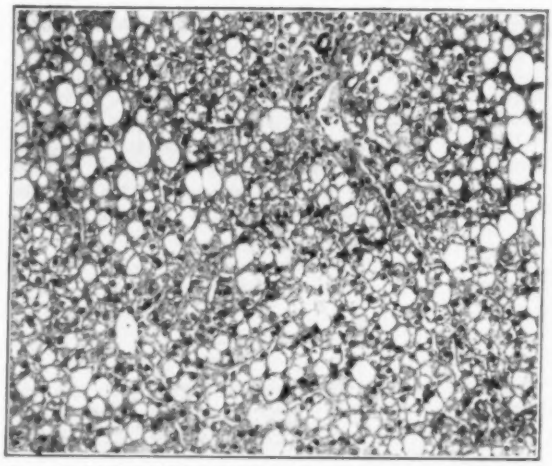

FIG. 1.—Liver. (H.E. ×125.) There is moderate to severe fatty degeneration, but no necrosis, fibrosis, or cellular infiltrate.

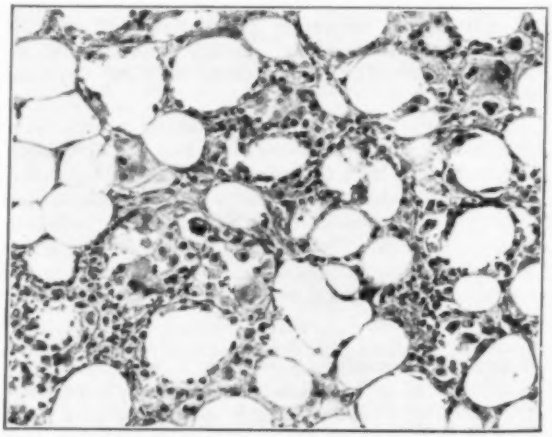

FIG. 2.—Subcutaneous fat. (H.E. ×125.) Varying sized foci of reticulo-endothelial cells lie between the fat cells. The macrophages have a foamy cytoplasm and some are multinucleate.

nor fever. The liver remained enlarged 6 cm. below the right costal margin, but there has been no worsening of liver function, as indicated by biochemical tests: serum bilirubin 0.3 mg./100 ml.; serum cholesterol, 230 mg./100 ml.; serum alkaline phosphatase, 10.7 units; thymol turbidity, 8.5 units; serum zinc sulphate, 10 units; serum albumin, 3.6 g./100 ml., serum globulin, 4.2 g./100 ml. A needle-biopsy of the liver performed on November 7 showed microscopically no significant change compared with the tissue previously obtained at laparotomy.

Discussion

The common clinical features of the syndrome as it affects the skin have been well recorded, and the title of the disease describes the characteristic triad of pyrexia which varies widely in degree, panniculitis, and the tendency to relapse. The term panniculitis, according to Stockman (1911) and Bain (1912, 1925), was originally introduced by Salin, of Stockholm. By it is meant inflammation of the panniculus adiposus—namely, the superficial fascia of the body covering, which is more or less impregnated with fat. The disease is rare, but widespread throughout the world. Although to date little more than 50 cases have been reported (Shuman, 1951), undoubtedly the disease is much commoner than this would suggest, even allowing for the fact that a number are buried under other names. Obesity is common but not invariable. Most of the reported cases have been in adult women, as in our case, but the disease can also occur in the young, as in the case of a 3-year-old boy described by Sosa Bens *et al.* (1955).

The panniculitis presents as subcutaneous nodules or plaques, adherent to the overlying skin, which appear most commonly on the thigh, although they can involve either extremity and the trunk, particularly over the back and abdomen. They vary in size from a few millimetres to several inches in diameter, characteristically tend to appear in crops, may be painless or tender, and are frequently erythematous, as in our case. There is a tendency for the affected subcutaneous tissue to atrophy, resulting in a depression of varying depth, and often a pigmented scar results. At times these scars may completely disappear spontaneously, as in our case, although this is uncommon. As the title implies, true suppuration does not occur, and the continuity of the skin is almost invariably unbroken, but in a few patients the lesion may become necrotic and break down to discharge a sterile yellow-brown fluid full of fat globules (Beerman, 1953). In some patients the disease is ushered in by an acute attack of nausea, vomiting, and abdominal pain, usually attributed to gall-bladder disease (Koch, 1951), and in many joint pains with swelling and tenderness occur, as in our patient.

The histological changes are non-specific. The process involves the entire subcutaneous fat nodule. DeLor and Martz (1955) recognized three phases histologically. In the first there is an inflammatory reaction in the adipose tissue, with oedema, congestion, and infiltration with polymorphonuclear leucocytes, lymphocytes, and macrophages. The macrophages have been variously called lipophages, histiocytes, polyblasts, granuloma cells, or foam cells. In the second phase there is necrosis of the fat cells and phagocytosis of the fat by macrophages. Sometimes these clump together and their cytoplasm coalesces to form multinucleated giant cells. In the final phase there is atrophy of the fat with connective-tissue replacement, but fibroblastic stimulation is very limited as a rule, although on rare occasions considerable replacement of fat by young connective tissue may occur, as in Christian's original case (his Fig. 8). Vascular changes are uncommon, although both periarteritis and endarteritis may at times be present, and sometimes the latter is considerable, as in our case. Fatty-acid crystals are not seen. Bailey (1937) is of the opinion that a histological feature not previously emphasized is the tendency for the interlobular connective tissue septa to retain the same width throughout.

Involvement of Organs other than Skin

Until recently the disease was thought to be confined to the panniculus adiposus and was therefore mainly of interest to dermatologists. It is true that in most patients the lesion is limited to the skin and is rarely lethal, and, of nine other examples of the disease which we were able to collect, seven of which were confirmed by biopsy by Professor H. A. Magnus, none had evidence of visceral involvement. Even when fatal, death is usually due to intercurrent disease, particularly infection. However, in a few cases not only may various viscera and other organs be involved in the same pathological process, but by being so may result in the patient's death. For cases in which the disease is not limited to the skin Steinberg (1953) has suggested the name "systemic nodular panniculitis," recognizing that it occurs in regions where there is no panniculus but employing the term in default of a better.

We have listed examples where visceral and other involvement has been specifically mentioned, in addition to our own case (see Table). The most extensively involved case which we have been able to find is that of Ungar (1946). It occurred in a woman aged 37 who died of acute suppurative peritonitis for which no local cause could be found, although it was presumed to have come from a

Systemic Weber-Christian Disease

Authors	Organs Involved	Special Symptoms and Signs	Other Remarks
Miller and Kritzler (1943)	Liver, spleen	Died of hepatic insufficiency	First necropsy report: acute focal necrosis of liver and spleen
Baumgartner (1944)	,, ,, heart		
Spain and Foley (1944)	Mesentery, omentum, and peritracheal tissue		Older lesions showed some fibrosis
Friedman (1945)	Liver, spleen, heart		
Ungar (1946)	See text		
Mostofi and Engleman (1947)	Liver, epicardium, peripancreatic, periadrenal, perirenal, and mesentery		
Jones *et al.* (1950)	Liver		Fatty necrosis and fibrous bands
Hanrahan *et al.* (1951)	,, spleen	Fatal within 3 months of onset	Liver wt. 3,400 g. Severe diffuse fatty metamorphosis
Bjornstad (1951)	,, marrow	Macrocytic anaemia	Liver wt. 1,670 g. Numerous rice-sized yellow fatty nodules
Kinmont (1952)	,, spleen	Liver-function tests impaired	
Schwartz *et al.* (1952)	,, ,, heart	Size of liver, spleen, and heart waxed and waned. Systolic murmur, regular rhythm	? Pericardial effusion. No necropsy
Steinberg (1953) Case 1	Peritracheal, pericardial, perihepatic, perirenal, and periadrenal tissue; submucosa of gastro-intestinal tract, bone marrow, mesentery, and omentum		
Case 2	Liver, spleen, periadrenal, perirenal, renal pelvic, myocardial, marrow, and pancreatic adipose tissue		
DeLor and Martz (1955)	Bone	Swollen red painful fingers and toes, with cystic destruction radiologically	Amputation of inflamed right 4th toe
Sattler and Greenberg (1956)	Mainly small-bowel adhesions	Bowel obstruction resulted, tarry stools	Successful resection of 44 cm. of terminal ileum

streptococcal tonsillar infection. In addition to typical skin lesions most of the adipose tissue throughout the whole body was involved, predominantly that of the retroperitoneal space. The pathological process included the true pelvis, mesentery, and omentum, and the lesions were most fully developed in the pararectal, mesosigmoid, mesenteric, and omental adipose tissue and around the kidneys and adrenals. The disease was also found in the anterior inferior mediastinum and in the subepicardial adipose tissue between the root of the aorta and the left auricle. Clinically, she had experienced both precordial and abdominal pain, and per vaginum the pelvic wall was felt to be lined by nodular formations which repeatedly changed in size between attacks of pain.

Hepatic involvement has not been particularly emphasized previously so far as we have been able to ascertain. In any toxic or infective process moderate fatty changes in the liver are to be expected, and, in fact, are commented on by several authors. However, it appears that, quite apart from such relatively slight changes, there is no doubt that occasionally gross fatty metamorphosis can take place in the liver as well as in other organs and give rise to considerable enlargement. Our patient still has enlargement of the liver, but is apparently well and has been apyrexial since her discharge from hospital. So far as we have been able to trace, she is the only example where prolonged pyrexia and hepatomegaly preceded the typical skin lesions. Examples of single cases with considerable hepatic enlargement are those of Baumgartner (1944), Friedman (1945), Mostofi and Engleman (1947), Hanrahan *et al.* (1951), and Schwartz *et al.* (1952).

Among causes to which the disease has been attributed are halogens used therapeutically, both bromides and iodides, infections both general and focal, allergy, and trauma, but in most cases there is no obvious cause. Bendel (1949) suggests that the allergy may be bacterial, chemical, or even of virus origin, and that it produces metamorphosis in the fat. This metamorphosed fat then acts as a foreign body in the tissues and calls forth an inflammatory reaction. It does not seem to be a primary disturbance of lipid metabolism, in that almost invariably there are normal values for total blood lipids, cholesterol, and cholesterol ester, and the disease is rarely distributed over most of the body.

Our patient had not received any halogens, we could find no evidence of infection, and trauma could be excluded, for she was under observation in bed at the time of the appearance of the panniculitis. Diabetes mellitus has also been described in association with Weber–Christian syndrome (Machacek, 1948), but her glucose-tolerance test was normal.

The outlook depends chiefly on the causative disease, if such can be ascertained. Remissions can occur. Christian's original patient had a remission of three years' duration, and one patient was free of the disease 20 years after the initial diagnosis—see discussion at the end of the paper by Miller and Kritzler (1943). In the case of Tilden *et al.* (1940), the patient died from miliary tuberculosis. Miller and Kritzler (1943) described the first necropsy to be made in the active stage of panniculitis, and their patient died of general debility with signs of liver insufficiency, and at necropsy acute focal necrosis of the liver and spleen with moderate fatty degeneration of the liver was found. Similarly, Bjørnstad's (1951) patient died of cirrhosis and fatty degeneration of the liver, accompanied by macrocytic anaemia. In the case of Spain and Foley (1944) death was due to glomerulonephritis. Friedman's (1945) patient died of staphylococcal septicaemia, and Ungar's (1946) patient of streptococcal peritonitis.

From the histological point of view the differential diagnosis is wide, as the microscopical changes are not specific and can result from a variety of conditions causing mechanical or chemical damage to the subcutaneous fat. Many of these can be ruled out clinically from the history alone. Among them may be mentioned subcutaneous fat necrosis of the newborn, insulin fat atrophy, paraffinomata, ischaemic fat necrosis, and traumatic fat necrosis of the breast. Clinically the syndrome is so characteristic that there are only two other conditions with which it may be reasonably confused, and one of these is probably nothing more than a variant of the disease itself—namely, the Rothmann-Makai syndrome. According to Baumgartner and Riva (1945) this syndrome is more common than Weber–Christian disease, and the patients differ in that they do not have any constitutional upset or pyrexia, and the nodules do not develop in typical attacks or crops and are usually smaller and so deep in the subcutis that they are seldom adherent to the skin and recede without local atrophy. Even so, Beerman (1953) is of the opinion that this distinction is an artificial one. Rare types of thrombophlebitis may also lead to difficulty in diagnosis, as pointed out by Barker (1934), and in such cases it may be necessary to look for histological evidence of thrombosis or inflammatory reaction in the vein wall.

Summary

Attention is drawn to examples of Weber–Christian disease in which, in addition to involvement of the skin, the liver, spleen, heart, bone marrow, and other tissues have been affected.

An example is reported with gross hepatomegaly and anaemia. The visceral involvement appeared eleven weeks before the typical skin lesions, a most unusual feature rendering early clinical diagnosis impossible. During the illness a hypochromic anaemia developed which could not be accounted for other than by the disease itself. At laparotomy severe fatty degeneration of the liver was found. It seems highly probable that the skin and liver were involved in the same pathological process, and possibly the bone marrow also. Her rheumatic heart disease was presumably incidental.

It is suggested that the syndrome may well be a sensitivity response of the reticulo-endothelial system which, although most commonly borne by the skin, can infrequently affect other organs.

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STRESS AND DISEASE: A REVIEW OF PRINCIPLES

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Definitions

The term "stress" is here taken to mean the internal or resisting force brought into being in the human organism by interaction with the environment (Wolff, 1952). In Western society one of the most important forms of such interaction in the production of illness is that between man and his fellow-beings. The stresses arising from this source are manifested in disturbances of thought, feeling and behaviour, and in disturbances of bodily function and structure. These may be brief and insignificant, or so persistent and troublesome as to constitute an illness. The group of illnesses in which stress is a principal factor in aetiology may be collectively termed the stress disorders.

It will be taken as an axiom that the aetiology of every illness is complex, and that many agents in both the mental and physical spheres enter into the causation of each disorder. In no case of illness are all these variables known, and the best that can be hoped for is an approximation to the truth. For instance, it may be difficult or impossible to appraise the causal influence of genetic endowment in the production of a particular disorder. It is fair to say that there are as many gaps in our understanding of the "organic" aspect of human reactions as in our insight into the emotional aspect. For instance, there is no general agreement about the physiology of the normal menstrual cycle. In the life history of a patient, one of whose bodily responses to stress is menorrhagia, the chain of events *situation–stress—symptom* may stand out so clearly as a recurring pattern as to leave no doubt about the linkage, yet the neural or endocrine mechanism of the response is still obscure. The "pathology of the whole person," in Balint's (1957) phrase, has still to be written.

A stress disorder may be defined as an illness which (1) begins at a time of crisis in the patient's life, (2) shows a time correlation with situations provoking stress in the patient, and (3) clears up when the situation changes or the patient learns to adapt to it better. To include under this heading a disorder such as urticaria is not to imply that urticaria is always and in every individual a stress disorder; in some individuals it certainly is, and thorough study of even a few of these should remind us that any investigation of urticaria which omits an appraisal of the stress factor is necessarily incomplete.

A Biological View of Illness

The biological view may be contrasted with the mechanismic (Halliday, 1948). According to the latter view, the human organism is a machine composed of mutually adjusted parts working together. Illness results from a breakdown in the machine, and the cause of illness must lie in a fault, disease, or imbalance in one or more of the parts. A list of the causes of illness is thus a list of faulty parts or local lesions. The doctor's task, in this view, is to discover and remedy the fault, and the more he knows about mechanism the more effective he will be.

The mechanismic view has in its time provided the framework for most of our present knowledge of the physics and chemistry of the body, and for understanding the processes of certain sorts of illness—for example, the infections. Its conceptual structure does not, however, enable the observer to comprehend in full the meaning of events occurring in a disorder such as recurrent vomiting in children associated with a rage reaction. Here there is no bodily fault or lesion; the machine is working well enough, but the person is in trouble.

On the biological view, illness can occur when the individual, predisposed to react in certain ways by his life experiences, encounters a situation to which he cannot readily adapt. The situation itself may not be especially dangerous or stimulating, but if the individual sees it as such and cannot take appropriate action stress is aroused in him; the form of mental and bodily response which he then shows will be determined by his physical constitution, his personality pattern, and the nature of the situation.

Stress responses, then, appear in the organism when circumstances urge to action, but no action is taken. The discharge of anger in words or behaviour, the working-through of grief by an explicit mourning, seeking of an appropriate outlet in states of sexual tension, reduction of anxiety by internal or external changes—these are examples of "resolution by action." When the source of stress is outside conscious awareness (as it so often is) or when action is blocked by inner censorship or outward restraints, there follows disharmony in the organism which may issue in symptoms of illness. There seems to be some variation from one person to another, and from one culture to another, regarding the degree of tolerance of this disharmony; this may perhaps be explained by differences in individual experience.

Common Stress Disorders

A provisional list of the disorders commonly met with in practice is as follows:

Group 1: Simple anxiety states, acute and chronic. Reactive depression. Simple hypochondriasis.

Group 2: "Effort syndrome." Palpitation. Dyspnoea out of proportion to degree of fitness. Left inframammary pain.

Group 3: Over-eating. Under-eating. Anorexia nervosa. Recurrent vomiting. Nervous diarrhoea. Constipation. Ulcerative colitis. Duodenal ulcer. "Abdominal discontent"—fullness, discomfort, wind. Recurrent abdominal pain.

Group 4: Giddiness, tremor, faintness, fatigue. Vascular headache. Insomnia. Malaise—feeling unwell, run-down.

Group 5: Urticaria. Neurodermatitis. "Eczema." Pruritus. Hyperhidrosis. Rosacea. Alopecia. Cheiropompholyx.

Group 6: Tension pain, in its various forms.

Group 7: Amenorrhoea. Menorrhagia. Period pain. Dyspareunia. Frigidity. Vomiting in pregnancy, after three months. Post-partum depression.

Group 8: Asthma. Vasomotor rhinitis. "Spots before the eyes." Amblyopia.

Stress may of course act as a contributory cause in other forms of illness besides these. For example, there are some people who become afflicted with a crop of boils when their resistance is low during a time of crisis. Indeed, for all we know, stress in some form may contribute to the causation of every illness. For practical purposes, however, it is convenient to bring together into one group the disorders listed above, since, in these, emotional tension is the principal determinant of symptoms.

Incidence

There have been few surveys of incidence of stress disorder in this country. Two of these are: (1) the study by Watts and Watts (1951), based on the examination of a year's work in general practice; the practice is one of 8,000 in a small country town (of 2,828 patients seen during the year, 316 (11.2%) were classed as "psychosomatic disorder"); and (2) Finlay and his colleagues (1954) reported a survey of incidence over one year by six general practi-

tioners, two working in the country, two in an inner metropolitan area, and two in an outer metropolitan area. Their results showed that, by and large, one-fifth of the patients seen on any day in an urban practice suffer from a stress disorder; in the country, the proportion will be 10–15%. Mestitz (1957), reviewing a series of 1,817 patients seen in a casualty department, commented that no "organic" cause could be found for 27% of the symptoms. His paper emphasizes the prime importance of pain as a presenting symptom. In 26% of those patients who gave pain as the main symptom, no physical basis for the illness could be traced; the treatment of these patients, the author says, was difficult and unsatisfactory. This is a usual finding among those who have to deal with tension pain.

Time Relations in Illness

In the recognition and understanding of a stress disorder one essential aspect for study is the relation of the illness to time.

First Appearance of Illness.—The time of first appearance of a stress disorder is never a matter of chance, and there is always a correlation between the point of emergence of the illness and the patient's emotional experience. This correlation may be quite manifest, as in the sequence *threat—fear—diarrhoea*, or it may be more obscure. The nature of the causal stress may be at first unknown to both doctor and patient, but in general the better the doctor knows his patient, and the longer the period of observation, the less likely is it that an attack of illness will remain unexplained.

Latent Period.—One difficulty in discerning the meaning of an attack of illness is that experience and attack may be separated by a latent period as long as 24 hours, or even more. For example, a patient prone to vascular headache commonly has his attack on Saturday or Sunday morning, when he is ostensibly at peace, the stress-provoking experience being an event on Thursday or Friday, or perhaps the accumulation of a week of heavy burdens.

Tempo of Illness.—Responses to stress may be divided into categories according to the rate of reaction. In skin disorder, for example, itching is a "fast reactor"—during a spell of rage the skin can begin to itch directly; whereas psoriasis is a "slow reactor"—changes in the size and colour of psoriatic patches follow the course of life-experiences, but in a leisurely way.

Time Correlation of Attacks.—The "Meyerian chart" is a simple device for recording the history of a stress disorder. It has three columns—one for the date, one for the attack, and one for the events surrounding the attack. The patient fills in the chart at his leisure, perhaps with the assistance of his wife, recalling as much as he can of the circumstances of each attack. A glance at the third column will then often show at once that there is a single thread connecting all the events associated with illness—for example, the patient takes ill only when some event occurs that provokes a particular reaction of guilt.

Curve of Recovery.—The course of recovery in stress disorder is seldom a straight line. Much more often it is of wave form, with remissions and relapses, the direction of the wave being towards normality. This curve is, of course, also much influenced by biological rhythms, such as the menstrual cycle in women, with its recurrent peaks of tension.

Mechanism of Symptom Production

The reactions of the body under stress are very diverse indeed, and there is scarcely any organ or system whose function may not be hastened or slowed or arrested or changed in some way. Wittkower (1928) showed that both joy and sorrow could increase the flow of bile from the liver, whereas annoyance stopped it altogether. The filtering function of the kidneys is impaired by prolonged anxiety. The working of the heart and blood vessels, and the gut, and in short all the internal organs, may be affected when the organism is exposed to stress. A formidable literature now exists in the field of psychophysical relations; some of the publications are summarized in each issue of the bimonthly American journal *Psychosomatic Medicine*.

The physical reactions in stress disorder are all produced through the agency of the central nervous system, but there are several possible mechanisms: (1) a direct nervous effect upon the organ or tissue, as when increased stimulation causes muscle tension and pain; (2) the glandular system acts as an intermediary agent; (3) bodily changes are produced indirectly, as when emotional tension provokes itching, the patient scratches and injures the skin, and a rash appears; (4) action by the patient, as when the diabetic omits his dose of insulin and goes into a coma; such action may of course be unconsciously motivated and purposive. These mechanisms may overlap or combine.

The response of the organism under stress, in an individual patient, may shift from one system to another. For instance, a woman with menorrhagia of emotional origin undergoes hysterectomy, since the bleeding cannot be controlled; during convalescence after the operation she begins to suffer from dyspepsia. This "switch of focus" is not uncommon, and it indicates that the underlying tensions have not been dealt with.

"Choice of Illness"

When the patient meets a situation which produces sustained anxiety in him, will this be manifested mainly by changes in mood and feeling, or mainly by physical symptoms, or both? And why one symptom or illness rather than another? These are questions which we cannot answer completely at the present time, though there are some indications where the answers may lie.

The factor of inheritance has always to be appraised. A particular illness often seems to "run in families." It is usually difficult, however, to separate the influence of inheritance from that of family environment.

The second factor is that of identification. The patient may take over from another person, especially someone to whom he is much attached, a bodily symptom or reaction-pattern. This process of "taking into oneself" the illness of another with whom we feel identified very commonly operates within a family.

A third factor is the presence of a vulnerable point. Suppose a man to have muscle tension higher than normal, but not enough to cause much pain; if he then slips on the stairs and "ricks" his back, and tension continues, the pain may thereafter centre on his back.

Structure and Function

Stress responses begin by being transient and reversible alterations in function, but, if they continue, changes in the structure of organs may follow. The classical example of this is bronchial asthma. The illness, which starts as a bronchial spasm in the anxious, over-protected child, may end with bronchitis, emphysema, and gross changes in bodily form. Asthma is one of the small group of stress disorders which are potentially lethal; another is ulcerative colitis.

Meaning and Purpose of Illness

One of the principal tasks of the doctor is to get hold of what is essential about the nature of an illness. The orientation of medical education in this country has been almost entirely towards the search for a physical pathology to "explain" the occurrence of disease. The doctor, faced with a situation of illness in an individual or a family group, may tend to look for events or data which can be understood in physical terms, since these are more tangible and have more meaning for him. Yet there may be an essential feature in the pathogenesis of an illness which is not in the physical field at all, and therefore is missed. Thus, a man has degenerative joint disease which gives him no trouble and is symptomless; then one day he reaches the limit of endurance with his wife, muscle tension rises and the joints become painful. This interpersonal event is highly meaning-

ful in relation to the onset of pain. There is a whole class of determinants of illness in stress disorder which belong not to the field of physical pathology but to the field of human passion and suffering.

A further consequence of mechanistic thinking in medicine is concentration on causes to the exclusion of purpose. In one sense all human behaviour, including illness, is purposive and directed at a goal. It is reasonable to ask, of any disorder, What is the biological purpose of this? We may take it that conscious malingering is very rare, and the answer to our question will not be found by inquiry from the patient, but only by an examination of the illness in its personal and social setting. Illness may be directed at protection of the patient from domestic chores, from sexual intercourse, from unwelcome duty; at competition with other ill people in the household; it may be used to appeal for help, to wield power over a superior, for blackmail or revenge, and for many other purposes. Where the purpose of illness is important in the patient's life-scheme, attempts to remove it will be vain and even hazardous.

Management of the Stress Disorders

With certain exceptions, one of which is tension pain, the results of skilled handling of stress disorders are good. In general, patients with these disorders want to get well. They will work with the doctor, and will tolerate the spells of anxiety that often accompany successful therapy. Low intelligence, gross emotional disharmony, and a life situation which is very unfavourable and cannot be altered—these count against improvement. The outcome of treatment will be much influenced by the meaning and purpose of the illness for the patient, and by the doctor's insight and patience.

Simple reassurance and emotional support are seldom enough, save in the simplest illnesses. The goals are ventilation of feeling and attainment of understanding of the illness and its causes; with these comes a renewed capacity for adaptation. Changes in the environment, occurring independently or brought about by the patient, may be essential to complete recovery. The choice of method—repeated interviews, emotional "abreaction" with the aid of drugs, hypnotherapy—will depend on the doctor's disposition and experience. Each of these methods allows the building up of that close contact between doctor and patient within which a new and better solution of life's difficulties can be worked out.

Treatment of the common stress disorders is within the compass of any doctor who is prepared to devote time and sympathy to it. In their second paper, Finlay and his colleagues (1956) showed that about half of a random series of patients with these disorders may be expected to show much improvement, or recover altogether, under the kind of treatment which a general practitioner can himself give; about half of the remainder will show some improvement. As only two of the entire series of more than a hundred were shown as "worse," deterioration of a stress disorder under general-practitioner care does not seem to be much of a risk. The medical student, working under supervision, is capable of undertaking effective treatment, and can learn a great deal from this experience (Goldman, 1955).

The Future

The proportion of stress disorder, relative to the other common illnesses, is unlikely to diminish as time goes on; on the contrary, it will probably increase. The following three fields need further exploration.

1. *Field of Investigation.*—For example, the incidence of stress disorder in various social groups, in hospital practice, and in industry; the physiological mechanisms of stress responses; experimental studies of organ reactions. A number of admirable and well-controlled studies have appeared in the *Journal of Psychosomatic Research*. The experienced general practitioner is in an especially strong position to carry out clinical inquiries into the natural history of stress disorder; his attitude will be that "blend of the human approach and the scientific outlook" which is so necessary in this kind of work (*Brit. med. J.*, 1957).

2. *Field of Management.*—The efficacy of various treatment methods needs to be tested out in practice on a larger scale than heretofore. The cost to the nation of the stress disorders, in terms of medical services, on the one hand, and reduced productivity in industry, on the other, must be very high indeed, to say nothing of the cost in human suffering.

3. *Field of Education.*—How best to prepare the medical student and the newly qualified doctor for the understanding and treatment of the stress disorders he will meet in his work—this is a crucial question which is occupying the thoughts of many educators both in this country and in America. My own view, for what it is worth, is that nothing can take the place of case-work in the teaching of psychotherapy. The handling of patients gives the student confidence and insight that are not easy to acquire in other ways.

In the words of Dr. Charles Newman (1957), it may be that the direction of evolution of medicine is towards "the understanding and control of the mind, and of the mental aspect of all diseases. . . . The safeguard of the future lies in medical education, provided that the one thing which is essential is maintained, the old professional spirit which has always underlain the practice of medicine in England, the spirit of putting the interest of the individual patient above the claims of gain, of fame, of research, and of the State."

Summary

A general review of the relationship between stress and disease is given. The terms employed are defined, and a list of the common stress disorders is proposed. An outline is suggested for these themes: time relations in illness, mechanisms of symptom production, "choice of disorder," and the concepts of meaning and purpose in illness. A note on therapy of the stress disorders and on the prospect for the future in medicine is added in conclusion.

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At a recent meeting at Strasbourg convened by the Council of Europe, public health experts adopted the text of a draft European agreement designed to facilitate the exchange between member countries of human blood and its derivatives (whole human blood, dried human plasma, human albumin, human gamma globulin, human fibrinogen). Under the terms of this agreement the contracting parties undertake to make therapeutic substances of human origin available to other participating countries who are in urgent need of them, subject, however, to the express condition that no profit is made of them, that they are used solely for medical purposes, that they shall be delivered only to bodies designated by the Governments concerned, and that they conform to the specifications laid down in an additional protocol to the agreement. It is further stipulated that the contracting parties shall take all the necessary measures to exempt from import duties the therapeutic substances placed at their disposal. Although the agreement is primarily concerned with the supply of blood and blood products, its provisions may be extended to cover other therapeutic substances of human origin. The draft instrument prepared by the public health experts now goes to the Committee of Ministers for approval.

ACROPARAESTHESIAE AND THE CARPAL TUNNEL

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The purpose of this paper is to describe the results of division of the transverse carpal ligament in 30 consecutive cases suffering from acroparaesthesiae. It was in 1893 that Schultze first used the term acroparaesthesiae to describe nocturnal attacks of severe pain and tingling that affected the hands of middle-aged women.

In our experience the patients are not always female and not always middle-aged, though usually they are both. In the great majority the pain and paraesthesiae are nocturnal—the patient waking from sleep with severe tingling in the thumb and fingers. The hand is usually described as swollen. There may be severe pain, burning or bursting sensation in the hand and digits, with a feeling of thickness or stiffness. The symptoms may be no more than a minor discomfort, but may be so severe as to prevent sleep, the patient getting up to pace the bedroom floor, rubbing and moving the hands and fingers. After several minutes of this treatment the symptoms tend to subside. Often the patient is completely free of symptoms during the day.

McArdle (1951) was the first to suggest that compression of the median nerve in the carpal tunnel by the transverse carpal ligament was the cause of this syndrome.

In 1945 Walshe propounded the view that it was due to stretching of the lower component of the brachial plexus over the first rib. He stated that wasting and sensory loss do not occur. In 1951 and 1955 he still adhered to the view that this is the cause in at least the great majority of cases. Ford (1956) called the condition the tired-arm syndrome, and suggested that it arose from an accumulation of metabolites in fatigued muscles. Martin and Elkington (1955) considered it to be an entity in itself but listed several differential diagnoses, including median and ulnar nerve compression, and said that acroparaesthesiae may occur in the lower limbs. The axillary inlet syndrome and cervical spondylosis are also conditions which have been considered possible causes of this syndrome.

On the other hand, Kremer *et al.* (1953), Garland *et al.* (1957), and Heathfield (1957) were all of the opinion that McArdle's view was correct, and described cases where the symptoms had been completely relieved by division of the transverse carpal ligament. It appears probable, therefore, that a difference of opinion still exists on the causation and treatment of this condition, and we feel that publication of the results of 30 cases in which the transverse carpal ligament has been divided is of value.

Results

Of the 30 patients 6 were male and 24 female. The ages of the men were 36, 74, 49, 62, 27, and 20. The ages of the women were: 30–39, 4; 40–49, 11; 50–59, 7; 60+, 2. The youngest woman was 32 and the oldest 70. The following table gives details of the cases.

Symptoms	(*a*) Mainly or wholly at night	26
	(*b*) ,, ,, ,, in the day	4
Limbs affected	Right	13
	Left	7
	Both	10
Changes on C.N.S. examination, apart from affected arms		Nil
(*a*) Wasting in thenar muscles		4
(*b*) Slight but objective sensory impairment		13
(*c*) Pain referred above wrist to arm		14
X-rays cervical spine		28
Slight lipping		9
Well-marked osteoarthritis		4
Cases submitted to surgery		30
(*a*) Number of operations		34
(*b*) Immediate relief of symptoms		33
(*c*) Nerve examined		10
,, compressed		6
,, not examined		20

It will be seen that the great majority of our patients were women and that most of them were middle-aged. Division of the transverse carpal ligament was performed on 34 arms in 30 patients. In 33 relief of pain and paraesthesiae was immediate. Where wasting was present (4 cases) this took many months before it finally disappeared. The sensory impairment (13 cases) was in no case severe and tended to recover more quickly than the wasting.

Of the 10 bilateral cases, four had the operation done on both sides with complete success; two are awaiting operation on the other side. A further two did not consider the remaining symptoms severe enough to warrant having the second operation. Of the last two cases, one had immediate relief in the hand operated upon, and in a few days complete relief in the other hand as well. The second operation here was not unnaturally refused. It is interesting that definite wasting was still present in the thenar muscles of the hand not operated on 18 months later, though the patient was symptom-free and the thenar muscles of the other hand were normal.

The single case recorded as a failure was one in which the operation was done with the faint hope that some relief might be obtained. The patient was a woman of 49 with pain and slight swelling and cyanosis of the fingers, hands, and feet. She was thought to have erythromelalgia (see Price, 1950), but had some worsening of the pain and paraesthesiae in bed at night. The condition was of long standing and gradual onset. The operation was performed on one hand with doubtful benefit and was considered to be not worth while repeating.

X-ray films of the cervical spine were taken in 28 patients. Thirteen were abnormal, nine showing slight changes and four considerable changes of osteoarthritis. In the light of the results of our treatment, these changes would appear to be fortuitous, not playing any part in the production of the symptoms.

In eight patients we found a local pathological condition which might originally have played some part in the onset of the condition. Three had osteoarthritis of the carpal and finger-joints (Kellgren and Moore, 1952), one was the patient with erythromelalgia, one had had a Colles fracture on the same side, one an ununited scaphoid fracture with some osteoarthritis, and two gave a history of hyperextension strain of the wrist. However, on examining this question of local disease more closely it really seems to have little bearing on the syndrome except in rare cases.

Reviewing our bilateral cases again, we found that two had had a wrist strain which in both cases was unilateral. One had a Colles fracture and another a fractured scaphoid; again in each case the possible local factor is unilateral in a bilateral case. Of the remaining four bilateral cases with local disease one was the case of erythromelalgia, previously mentioned, and one had osteoarthritis in the small joints of the hand on one side only; the other two had bilateral osteoarthritis of the small joints of both hands, but, whereas one had bilateral symptoms, the other, with equally severe osteoarthritis, had only unilateral symptoms.

We found pain referred to the arm above the wrist in 14 cases. It was on occasion felt as far up as the shoulder. The following is an illustrative case.

This patient had typical nocturnal paraesthesiae in the left hand. She also had wasting of the thenar muscles of moderate degree and impairment of sensation to pin-prick and light touch, not confined to the median area but extending up the radial side of the forearm almost to the elbow. An area of sensory impairment of this size seemed to rule out carpal tunnel compression, but in view of the typical symptoms the transverse carpal ligament was divided. The symptoms were immediately relieved; wasting and sensory impairment cleared up slowly over some months—eventually completely.

Garland *et al.* (1957) say that they compressed the anterior aspect of the wrist digitally for three minutes in five patients and reproduced typical acroparaesthesiae in three. One of us (F. R. Z.) used a similar test. Firm pressure over the transverse carpal ligament for one to three minutes reproduced the typical paraesthesiae in 22 out of 27 patients in this series. However, the most important single diagnostic feature was tingling often amounting to pain in the thumb and radial three fingers, worse in bed at night, and improving after the patient had been up and about for several minutes. Where this history was given, division of the transverse carpal ligament brought complete relief of symptoms even if the pain present in the arm had spread as far as the shoulder.

Discussion

From our experience and also from that of Kremer *et al.* (1953), Garland *et al.* (1957), and Heathfield (1957) it is clear that the original description must be widened to include cases which, while having the typical pain and paraesthesiae, also have wasting of the thenar muscles, impaired sensation in the median area, and pain spreading upwards from the hands even as far as the shoulder.

In 1947 Brain *et al.* described six cases of compression of the median nerve in the carpal tunnel. At least three of these cases had the typical acroparaesthesiae as well as wasting of the thenar muscles and sensory loss. It would appear that these represent more severe cases of the "acroparaesthesiae syndrome."

The onset of the syndrome is often associated with undue fatigue—for example, after carrying very heavy shopping baskets. It therefore seems possible that some form of compression of the venous return is taking place at the thoracic inlet, giving rise to undue swelling of the soft tissues distal to the carpal ligament.

Three years ago we saw a woman with typical acroparaesthesiae. The symptoms had been present only three weeks and cleared up completely with rest. Four months ago we again saw this patient with severe acroparaesthesiae in the right hand, much less in the left. She also had severe pain in the forefinger which was present day and night and prevented sleep. Instead of the normal joints and hands of three years before, she now had the typical early menopausal rheumatoid type of arthritis with a good deal of soft-tissue swelling in the hands and wrists. The pain was so severe that the right transverse carpal ligament was divided. There was immediate relief of the severe pain and paraesthesiae, though the rheumatoid process remained unchanged.

This case is not included in the above series as insufficient time has elapsed for a follow-up. It seems fairly clear in this case that soft-tissue swelling below and distal to the carpal ligament was to some extent responsible for undue pressure on the median nerve by the carpal ligament. Why, therefore, do we not see this syndrome more commonly in rheumatoid arthritis? Whether any such mechanism as this plays a part in producing symptoms in what appears to be an otherwise normal hand is at the moment speculative, but there can be no doubt that our results strongly support McArdle's (1951) original view.

Summary

In 30 cases of acroparaesthesiae the transverse carpal ligament has been divided in 34 wrists. In 33 there was immediate relief of pain and paraesthesiae. In the remaining case some other pathological condition was present.

Wasting of the thenar muscles, impairment of sensation, and pain referred to the arm, even as far as the shoulder, have been present in these cases—apparently successfully treated by division of the anterior carpal ligament.

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Medical Memoranda

Fatal Case of Agranulocytosis Due to Chlorpromazine

Jaundice and photosensitization of the skin are well-recognized complications of chlorpromazine therapy. Neutropenia and agranulocytosis occur more commonly in cases treated with another phenothiazine compound, pecazine ("pacatal") (Mitchell *et al.*, 1957), but at least two fatal cases of agranulocytosis following treatment with chlorpromazine have already been reported (Tasker, 1955; Pollack, 1955). A brief account of yet another fatal case of agranulocytosis following treatment with chlorpromazine is given below.

CASE REPORT

The patient, a man of 47, was formerly a collier and later a pottery worker. He developed symptoms of schizophrenia while serving in Egypt in 1943, and was sent back to England shortly afterwards. He was an in-patient at St. Edward's Mental Hospital, Cheddleton, almost continuously since then. He was disturbed by visual hallucinations, laboured under various delusions, and attempted to commit suicide. No remission or improvement of his mental symptoms occurred. A blood count taken on March 29, 1957, was quite normal. Next day treatment with chlorpromazine was begun, starting with 75 mg. daily and gradually increasing to 300 mg. daily. On June 17, while still receiving the same dosage, he developed a sore throat and a pyrexia of 104° F. (40° C.). His white cell count was 250 per c.mm., with complete absence of neutrophils. A diagnosis of agranulocytosis was made, the drug withdrawn immediately, and treatment with penicillin instituted. As his general condition deteriorated he was transferred to the City General Hospital, Stoke-on-Trent, where on arrival on June 19 his blood count showed 105% haemoglobin (15.5 g./100 ml.), with a total white cell count of 300 per c.mm. and a complete absence of neutrophils. Jaundice and bronchopneumonia supervened 24 hours later, and he died on June 21, four days after the onset of symptoms.

Necropsy, performed 22 hours after death, revealed generalized icterus of skin, sclerae, and most of the internal

organs. The liver (weight 2,090 g.) was somewhat enlarged and oedematous. Microscopical examination showed mild fatty degeneration and a scanty infiltrate of lymphocytes in the portal tracts. The trachea and main bronchi contained mucopus, and both lobes of the left lung were consolidated. The microscopical picture was that of pneumonia, though only very few polymorphs were found in the inflammatory exudate. There were numerous ulcers in both tonsils and at the base of the tongue. Histological sections showed massive necrosis in the floor of these ulcers, but again there were only very few neutrophils. The bone marrow of the sternum, the vertebral column, and several long bones appeared normal to the naked eye, but smears and sections revealed a complete absence of all myeloid cells, with the exception of a few scattered promyelocytes and eosinophilic myelocytes. The bulk of the cells were erythroblasts and lymphocytes, with a normal distribution of megakaryocytes.

COMMENT

The cause of death was undoubtedly agranulocytosis and pneumonia. Jaundice develops in many cases of agranulocytosis from all causes, usually as a terminal event. It is therefore difficult to say in this case whether it was due to liver damage from chlorpromazine or to the agranulocytosis.

It is generally agreed nowadays ("Any Questions," 1957) that regular blood counts can do little to prevent agranulocytosis due to drug therapy. The present case therefore underlines once again the need for caution in the administration of drugs of the phenothiazine group.

Our thanks are due to Drs. C. H. Catlin and J. H. Molloy, under whose care the patient was admitted.

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Intra-articular Prednisolone

Although prednisolone (Δ^1-dehydro-hydrocortisone) has been available for systemic administration for several years, it is only recently that it has been prepared in a form suitable for intra-articular injection.

So far only three reports have been published on its use by this means. Hagedorn (1957), in surveying the results of its administration to 89 patients suffering from various joint and periarticular soft-tissue lesions, concludes that it produces the same effect as hydrocortisone in less than half the dosage. Moreover, he states that it is completely free of the local exacerbation of symptoms that is known to follow the local use of hydrocortisone in 25 to 30% of cases. On account of this complete absence of subjective and objective side-effects, the small doses needed, and the fact that the effect of prednisolone is equal to that of hydrocortisone, he concludes that it is the drug of choice. Thompson (1957) and Newton (1957), although not quoting the number of cases subjected to trial, suggest that there is no significant difference between prednisolone in its acetate or higher ester form and hydrocortisone, although Thompson considered that the results were significantly better when it was injected into the small joints of the hand.

PRESENT INVESTIGATION

In view of this apparent contradiction of evidence the results of a short controlled trial of prednisolone acetate ("hydrodeltalone") in 79 patients suffering from rheumatoid arthritis are recorded. The difficulty in assessing results in this condition was to some extent eliminated by confining the trial to the elbow- and knee-joints, both of which are readily accessible to measurement of joint swelling, joint temperature, and range of movement. The trial was also confined to joints in the acute stage, as, although the steroids could be expected to produce only a temporary relief of symptoms, this period of relief could be accurately measured in days or hours. Eighty patients were accordingly selected and injected with equal doses (25 mg.) of either hydrocortisone or prednisolone acetate at random. After the effect of one injection had been judged to have worn off, the other steroid was injected. At the time of the injection with the prednisolone the patients were not told that a "new drug" was being tried, and to all external appearances the content of the syringe appeared the same in each case.

Every patient was asked to give an assessment upon the speed of the effect, the incidence of local reaction to the injection, and the duration of the effect.

This inquiry was correlated with a subjective examination of the joint involved to estimate improvement in swelling and range of movement.

Results.—Of the 80 patients treated in the manner described, one failed to return for assessment and six have been excluded from analysis as they failed to show any response to hydrocortisone, although all responded to the prednisolone. The results in the remaining 73 patients are shown in the Table. The average onset of relief was 10 hours earlier in the case of prednisolone, the average duration of relief two days longer, and the incidence of side-effects 27% lower. There seemed to be little difference in the intensity of the effect between the two drugs in similar doses. Statistical analysis of the results by 2×2 contingency confirms the clinical impression that prednisolone produces the more rapid and longer duration of relief than hydrocortisone ($\chi^2 > 11$, $P = 0.001$).

Results

Drug	Average Onset of Relief	Average Duration of Relief	No. of Patients with Increased Joint Pain
Hydrocortisone ..	30 hours	6·5 days	38
Presnisolone ..	20·3 ,,	8·1 ,,	15

CONCLUSIONS

It would appear, therefore, that prednisolone acetate gives a significantly longer period of relief, a much lower incidence of local reaction, and a slightly more rapid onset of effect in the acutely inflamed rheumatoid arthritic joint than hydrocortisone acetate. That six patients responded to prednisolone who were resistant to hydrocortisone would suggest that the former might prove of value where such a resistance is already known to exist.

Although the present trial was confined to those suffering from rheumatoid arthritis, experience with 284 patients suffering from a wider range of articular and soft-tissue lesions suggests that this rapidity of action, reduction in the incidence of local exacerbation, and duration of effect can also be observed following local injection of prednisolone.

I thank Dr. E. J. Crisp, consultant to the department of physical medicine, Guy's Hospital, for permission to publish these results; Dr. W. J. Butterfield for assistance in the statistical survey of the figures; and Messrs. Ward Casson Ltd. for the generous supply of hydrodeltalone.

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Reviews

ORGANIC BRAIN DISEASE

The Clinical Examination of Patients with Organic Cerebral Disease. By R. Klein, M.D. (Prague), and W. Mayer-Gross, M.D. (Heidelberg), F.R.C.P. (London). Foreword by Sir Russell Brain, Bt., D.M., D.C.L., LL.D., F.R.C.P. (Pp. 96 +xiii. 15s.) London: Cassell and Co. 1957.

The disturbances of behaviour which may occur in organic disease of the brain are of great interest to neurologists and psychiatrists, and to analyse them adequate and systematic examination of the patient is necessary. Examination of these higher functions is often neglected, partly because it usually takes a good deal of time and partly because the best methods of demonstrating specific defects are not widely known. Dr. Klein and Dr. Mayer-Gross have written this short book to remedy the latter deficiency. They describe in some detail the most useful clinical methods of investigating aphasia, agnosia, apraxia, disturbances of the body image, and related disorders. The various tests are succinctly described, and if these are carried out systematically the physician will learn a great deal about the type of behaviour disturbance shown by his patient. The authors indicate rather briefly the conclusions which may be drawn from the way in which a patient carries out the tests, but they do not discuss in any detail the more debatable aspects, such as the theories of aphasia and cerebral localization. Their statement that the length of retrograde amnesia usually "goes parallel" with the severity of brain damage in a head injury is not generally accepted, as many neurologists consider that the period of post-traumatic amnesia is a more useful indication; retrograde amnesia may contract to a very short period even when a closed head injury has been of some severity. There is an excellent list of references for further reading, many being in German and French, as the types of cerebral disorder discussed in this book have been extensively studied in these countries. This book fills a real need and should be of great assistance to all who are interested in organic disorders of the brain.

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CONFERENCE ON HORMONES

Hormonal Regulation of Energy Metabolism. Compiled and edited by Laurance W. Kinsell, M.D. (Pp. 242+xiii. 40s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957.

This is the record of a conference, or symposium, held at the Institute for Metabolic Research in Oakland, California, with 19 participants from the U.S.A., Professor Houssay from Argentina, and Professor F. G. Young and Dr. P. J. Randle from Great Britain. Eight sections deal with energy hormonal aspects of carbohydrate metabolism, enzymatic activity, anterior pituitary function (two sections), thyroid, insulin (two sections), and the adrenal cortex. Each contribution is followed by a discussion, the former being far too short and the latter too long. It is therefore discursive rather than systematic, and references are too often absent or fragmentary. This presentation has obvious advantages and disadvantages. Reading is pleasant and personal, and the cut-and-thrust of debate and discussion lively, bringing the reader into the conference as if it were happening at the very moment. However, some colloquial phraseology seems a little Mark Twainish in a scientific conference. Thus: "I'm not sure what Dr. L. meant by cul-de-sac, but I know what I meant. That is, that the only way out is a reverse of the way in." These friendly comments should not detract from the originality of approach and the breaking of new ground that are evident in most sections, and that give the reader up-to-date knowledge and much material for thought.

Somewhat at random, here are points of attraction: Dr. Stadie described the preparation of isotopically labelled insulin for studies of the binding of insulin by tissues—(1) insulin sulphate, with ^{35}S in the sulphate group attached to aliphatic hydroxyl groups; and (2) insulin with radioactive iodine in the tyrosine residues. The activity of the bound insulin was found to be affected by disturbances of the endocrine state. As might be expected from the presence of Houssay, Young, and Randle, joined in discussion by Professor Best, two excellent sessions deal fundamentally with pituitary effects on metabolism, and the references are excellent. Houssay indicated the importance of species difference in measuring relative diabetogenic potency of growth hormone, prolactin, and A.C.T.H.; and considered that there are reasons other than calories for the adiposity that develops easily in hypophysectomized rats forcefully fed. Randle and Young referred to deposition of protein, enhanced katabolism of fat, and depression of carbohydrate utilization resulting from pituitary growth hormone; and the dependence of growth hormone on insulin for protein anabolism (Lukens and McCann; Salter and Best); also evidence from their own work that growth hormone may stimulate the release of a hyperglycaemic factor from the pancreas as well as insulin; the part-dependence of growth hormone on the availability of adrenal steroids in relation to the depression of glucose utilization; their experiments with insulin assays, concluding that in the intact cat "treatment with growth hormone leads to a rise in the insulin content of the blood, and that this results from a greater rate of insulin secretion by the pancreatic islets rather than from a reduction of the rate of insulin utilization or destruction." Correspondingly in man they found active acromegaly to be associated with increased plasma insulin. They refer to experiments showing that corticotrophin can induce a fall of blood sugar in intact mice (Kurtz *et al.*), although no increased insulin production by corticotrophin was demonstrable by their isolated rat-diaphragm technique. Growth hormone in rats is somatotrophic but not diabetogenic, although it depresses utilization of glucose by muscles and the conversion of glucose to fat. In a masterly summary of the complexity of the action of growth hormone Young and Randle seem to hold all theories, including their own, as incompletely conclusive and awaiting a vital link of substantiation.

I found the adrenal cortex section nebulous and disappointing and devoid of any scientific references. Nevertheless it included some interesting aspects. Thus Astwood suggested that "the liberation of amino acids from body protein is a response which comes nearer than any other to being a direct action of adrenocortical steroids." Dr. Kinsell referred to "initial relatively greater loss of phosphorus, indicating that the material broken down is a highly nuclear material." Houssay recorded work with Dr. Guspide in his laboratory to the effect that there was a 90% reduction in the adrenal secretion of 17-hydroxycorticoids within a few hours of hypophysectomy; and, recalling that he had performed 900 hypophysectomies in dogs in 45 years with 70% deaths in the first week, contrasted these results with 29 recent hypophysectomies with the use of cortisone after operation and no deaths.

No reader will fail to have his hormones and cerebration stimulated by this welcome record of a conference many of us would have enjoyed attending. S. LEONARD SIMPSON.

VENOUS ANGIOGRAPHY

The Salient Points and the Value of Venous Angiocardiography in the Diagnosis of the Cyanotic Types of Congenital Malformations of the Heart. A Ten Year Study of 421 Angiocardiograms Done on 283 Patients. By Benjamin M. Gasul, M.D., Gershon Hait, M.D., Robert F. Dillon, M.D., and Egbert H. Fell, M.D. (Pp. 80+x; illustrated. 25s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957.

The importance of angiocardiography in the diagnosis of many heart lesions has become increasingly apparent with the growth of cardiac surgery. In certain forms of heart disease, notably complicated congenital lesions, this investigation is essential if a decision is to be reached as to whether surgical treatment can be undertaken or not. The procedure is not without its dangers, and it requires complicated

apparatus and adequate technique to enable a reasonable interpretation of the films to be made.

In this work the authors do not concern themselves with the methods or technique, but confine their observations to the interpretation in congenital cyanotic heart disease. A series of 283 patients were studied, almost all of them children, and 421 angiocardiograms were undertaken (each averaging 20 films). There were no deaths. The cases are grouped into those that can be routinely diagnosed by this method and those that require some additional method to achieve diagnosis. Fallot's tetralogy, transposition of great vessels, and some forms of anomalous venous drainage should be capable of accurate diagnosis by angiography. Congenital mitral or tricuspid stenosis, pulmonary stenosis with a ventricular defect, and cyanosis of extracardiac origin cannot be diagnosed by this method alone; and between these extremes are such diseases as truncus arteriosus, pulmonary stenosis with a normal aortic root and an interatrial communication, which may be suggested by this method but cannot always be decided on definitely.

The diagrams and reproductions of radiographs are excellent, and the commentary and analysis of results indicate the value of this method in the individual condition. Though this small work is primarily based on radiology, it contains a great deal of valuable additional information, particularly in respect of pathological anatomy. Its chief asset and object is to indicate where the procedure must be used, where it may be used, and where its findings remain inconclusive.

T. HOLMES SELLORS.

HISTOPATHOLOGICAL TECHNIQUE

Handbook of Histopathological Technique (including Museum Technique). By C. F. A. Culling, F.I.M.L.T., F.R.M.S. Foreword by R. J. V. Pulvertaft, O.B.E., M.D., F.R.C.P. (Pp. 446+x; illustrated. 45s.) London: Butterworth and Co. (Publishers) Ltd. 1957.

This book is a welcome addition to books on pathological technique. It is based on the syllabus for the final examination in pathological technique of the Institute of Medical Laboratory Technology and covers in detail all the methods in regular use in pathological laboratories. Special procedures that are less often required but the principles of which should be known to technicians are dealt with in less detail. Medical museum technique and practical microscopy are well and adequately covered. No doubt individual pathologists would have placed different emphasis on different parts of this book, but it can be looked upon as representing up-to-date practice in pathological laboratories.

Methods are clearly described and the reasons for various procedures explained. The attention paid to practical details and to the description of pitfalls which are rarely mentioned in books reveal the author as an experienced technician and teacher. His anxiety to make himself clearly understood sometimes leads him to use more words than are necessary, and his choice of words is not always felicitous. It is important that the style of writing of a technical book should be as good as that of any other. Through constant use readers are influenced unconsciously and soon pick up bad habits—for example, the use of "mitose" for "divide" or "undergo mitosis."

The book is well planned and easy to use; it contains numerous tables, diagrams, and illustrations which are good and enhance its value. (Illustrations (*g*) and (*h*) in Fig. 32 are transposed.) A useful list of references is appended. The author and publishers rightly believe that, in addition to serving as a reference book and textbook for technicians, this book will be used at the bench. To that end the publishers have provided a special binding which is said to be waterproof and acid-resistant; perhaps it was an odd chance that a section of the review copy was not firmly bound and would not long have resisted bench use. It is from the bench rather than from the armchair that the book will be judged. It can confidently be recommended for general use by technicians and pathologists alike.

R. WILLIAMSON.

DOCTORING IN THE U.S.S.R.

Doctor and Patient in Soviet Russia. By Mark G. Field. Foreword by Paul Dudley White, M.D. (Pp. 266+xviii. 40s.) Cambridge, Mass: Harvard University Press. London: Oxford University Press. 1957.

This book of 250 pages primarily comes from the Russian Research Centre of Harvard University, but Dr. Field before completing it and submitting it for his Ph.D. thesis spent a period in the Soviet Union. The book deals with the problems of organization, the functions and training of the doctor, and the doctor–patient relationship. It contrasts the pre-1917 era and it shows the evolution up to the pre- and post-Stalin period. It is written entirely without bias; it is factual, very readable, and an excellent book for reference. The problem of how party loyalty conflicts with professional ability keeps constantly recurring, and there is a chapter alone on "To Certify or Not to Certify: the Physician's Dilemma." Dr. Field shows that, on the whole, the standing of the medical profession is below that of "prestige occupation." Its former power was reduced by the elimination of independent medical associations such as the Pirogoff Society and others, and by recruitment intentionally from the peasant classes. The low salary of the general practitioner compares unfavourably with other workers, being in some cases only half that of a coal-miner. Malingering appears to be more prevalent than one would expect in a totalitarian State.

The book is not so much a study of Soviet medicine as of the sociology of the medical profession. It explains why medical faculties, after being linked to a university for 200 years, suddenly became autonomous. It points out that in 1944 the medical students' course was lengthened to six years. Now in the Soviet Union there are some 310,000 doctors—that is, 16 doctors per 10,000 of the population, not very different from Britain or the U.S.A. In 1917 there was in Russia one-fifteenth of that number. The author finally points out that the medical profession and education stand closer to the heart of the Soviet citizens than any other branch of Soviet life.

IAN FRASER.

DRUGS FOR DERMATOLOGISTS

The Dermatologist's Handbook. By Ashton L. Welsh, M.S., M.D. (Pp. 427+xii. £5 12s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957.

This volume is something more than is usually understood by a handbook; it has over 400 pages and is large and unwieldy. Its purpose is to provide an "extra pharmacopeia" which lists not only the substances used for local treatment of skin disorders but a great variety of other drugs which might be used in the incidental treatment of dermatological patients. These include central nervous system depressants and stimulants; there is a section on tranquillizers, on skeletal muscle relaxants, on anthelmintics, and on cholagogues. These and a great many other substances are listed, their chemical and therapeutic purpose described, and a great number of prescriptions and formulae detailed, including the formulae of a large number of proprietary preparations. Unlike a handbook of therapeutics, the present volume does not consider in any detail the indications for treatment or the considerations which govern the choice of one medicament rather than another. For the most part the book is based on the *United States Pharmacopeia*. For these reasons this is hardly a book for daily use, but may prove valuable for occasional reference.

F. R. BETTLEY.

Antiseptics, Disinfectants, Fungicides, and Chemical and Physical Sterilization, edited by George F. Reddish (2nd edition; Henry Kimpton, London; pp. 975; £5 12s. 6d.), brings together and evaluates information on these matters. It is the work of 28 American authorities. Three new chapters in the second edition deal with methods of testing sanitizers and bacteriostatic chemicals, sterility tests and methods for assuring sterility, and ultraviolet irradiation as a germicidal agent.

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SWEET TOOTH AND DECAY

In one African tribe an attack of dental caries is considered sufficient grounds for divorce. If one of the children has decayed teeth he is forbidden to feed from the family pot; he sits forlornly in the corner of the hut and dines alone. Under these rules almost all the marriages in Great Britain would be broken and all but a few children would eat alone, for the incidence of dental caries is so great that scarcely have the teeth erupted before their destruction begins. On the average, a child aged 4 years has at least four bad teeth; each year through childhood one or two teeth are added to the total number affected. It surprises no one, therefore, that the dental profession, now entering the lean years of manpower shortage, is unable to restore more than a small fraction of the children and adolescents to dental health.

Dental research workers are agreed that the caries process is initiated by the products of bacterial activity. Masses of bacteria thrive in the mouth in places where food particles stagnate. These aggregations of many types of bacteria form sponge-like plaques into which seep solutions containing debris from food and drink. The bacteria in the plaques produce acid in one and a half minutes after a sweetened beverage has been taken. The strength of the acid and the length of time it remains undisturbed in contact with tooth enamel determines whether primary decalcification, the first step in the caries process, will take place. Other factors such as the individual resistance of the tooth substance, the buffering capacity of saliva, and its composition and rate of flow also play a part. In brief the bacteria which produce caries will thrive if they are provided with a constant supply of food. Carbohydrate debris on and around the teeth acts as a reservoir of food from which the bacteria produce the acid and the enzymes of destruction. It is interesting to note that, though the jaws may be well formed and the teeth perfectly arranged, favouring the rapid natural clearance of debris from the mouth, faulty eating habits can be disastrous. The advent of "civilized" foods into modern primitive communities such as the Eskimo tribes has proved this fact. The round-the-clock eating and drinking of sweetened drinks, biscuits, toffees, chocolates, in fact all carbohydrate foods, maintains bacterial activity and as a result the teeth are attacked. The effect is even worse in a mouth having irregularly arranged teeth and untreated cavities, for these areas of stagnation harbour more food debris. Thus the saliva, washing over the bacterial plaques, contains sufficient nutrients to support the bacteria even though the total intake may be less. Frequency of intake is the major factor.

Among the many reports which have shown the relationship of bacteria to caries, the animal experiments of F. J. Orland[1] and colleagues are interesting. Germ-free rats were raised under bacteriologically sterile conditions, and it was shown that bacteria and carbohydrate substances must be present to produce experimental dental caries. The classical research studies at the Vipeholm Hospital in Sweden[2] have shown conclusively that the risk of caries is greater when sugar-containing food and drink are consumed between meals. Further studies have indicated that when those sugar-rich foods are removed from the diet the incidence of caries is greatly reduced. A. B. MacGregor[3] condemns toffees as one of the most damaging types of confection, as also do the Swedish investigators. The physical consistency of toffee particles allows fragments to remain for hours impacted in stagnation areas and in the pits and fissures of the teeth.

A recent report from the Medical Research Council throws light on these problems. P. J. Holloway, M. Mellanby, and R. J. C. Stewart[4] describe an *in vitro* investigation into the effect on the teeth of fruit drinks, cordials, acidulated sweets and lollipops, iced lollies, Ministry of Health orange juice, rose-hip syrup, and bottled blackcurrant juice. All of these cause destruction of the teeth by erosion—that is, the loss of tooth surface by solution in acid. The *p*H of these drinks is very low, and erosion can follow contact with the tooth surfaces for short periods. This work is related to the report by P. M. C. James and G. J. Parfitt,[5] who observed a similar effect on the incisors of young children when dummies were dipped in various fruit juices. The erosion of the tooth surfaces predisposes to dental caries, and it is a common experience in everyday dental practice to relate rampant caries in the first dentition to the continuous intake of the confections described. The suggestion made by Holloway and colleagues that the *p*H of these preparations

[1] Orland, F. J., *et al.*, *J. dent. Res.*, 1954, **33**, 147.
[2] Gustafsson, B. E., *Acta odont. scand.*, 1954, **11**, 207.
[3] MacGregor, A. B., *Aust. dent. J.*, 1956, **1**, 195.
[4] Holloway, P. J., Mellanby, M., and Stewart, R. J. C., *Brit. dent. J.*, 1958, **104**, 305.
[5] James, P. M. C., and Parfitt, G. J., *Brit. med. J.*, 1953, **2**, 1252.
[6] Slack, G. L., Royal Society of Health Congress, 1958, in press.
[7] *Report of the Committee on Recruitment to the Dental Profession*, 1956, p. 38. H.M.S.O.

should be restricted to not less than 3.5 is sound, and it is hoped will not pass unheeded. Certainly the prescription of these fruit juices and sweetened supplements to the diet should include clear instructions on oral hygiene if the damaging local effect is to be avoided.

There are three main lines of approach to the prevention of dental caries: the elimination or inhibition of bacterial activity, the removal of the substrate, and the increase of tooth resistance to attack. All these are being thoroughly investigated; the effect of optimum fluoride intake during tooth development is one example of a method of increasing resistance to caries. Meanwhile enough facts are known on which to base helpful guidance in prevention, and parents, properly instructed, can contribute much to the avoidance of dental disease in their children. At the 1958 Congress of the Royal Society of Health simple rules for the maintenance of dental health were given[6]; (1) No eating or drinking between meals. (2) Regular mealtimes; a planned diet which allows the eating of chocolate and other sweetmeats only at table; the eating of fibrous fruits or vegetables such as apples or carrots at the end of meals to aid physiological cleansing of teeth. (3) The encouragement of children by example and instruction to use the bubble and swallow technique of rinsing the mouth with plain water three times after eating and drinking. (4) Instruction of young children in oral hygiene by parents and teachers showing the value of brushing the teeth, especially last thing at night.

It has often been observed that when families are able to keep to these rules the children remain free of caries. Some children are able to accept responsibility for their own dental health, but encouragement from those in authority over them is essential. It is nevertheless important to intercept dental caries in its earliest stages by dental treatment. The need for education in dental health on a national scale is generally admitted, and the McNair Report[7] makes a recommendation to this effect which deserves to bear fruit.

TREATMENT WITH PENICILLINASE

Penicillinase, an enzyme formed by several species of bacteria, which inactivates penicillin, has hitherto been regarded only as an obstacle in therapeutics, but in one direction it has now proved to be an asset. On the debit side is its interference with the therapeutic action of penicillin. Resistant staphylococci owe their resistance to their formation of this enzyme, which enables them to destroy the antibiotic in their environment. In mixed infections a penicillinase-forming species such as *Ps. pyocyanea* may nullify the action of penicillin on a highly sensitive organism such as a haemolytic streptococcus. This action has been suspected or proved in individual patients for years past: its reality has recently been neatly proved in experimental infections by R. Tacking.[1] This author[2] and W. Markov[3] have gone to the length of immunizing animals with penicillinase, or administering immune serum so produced, in order to neutralize the enzyme formed by resistant staphylococci at a site of infection, and so to enable penicillin to exert its normal effect. This proceeding was successful in animals, but does not appear to have been exploited in man.

Penicillinase can be useful only when the destruction of penicillin is actually desired. It has thus long been used in sterility tests of the antibiotic itself, and as an addition to cultures of body fluids containing penicillin. Another situation in which it would be highly desirable to denature penicillin if possible is when it is causing a reaction in a sensitized patient. That it might be applicable to this purpose occurred first to R. M. Becker[4]; he used a commercial preparation of penicillinase extracted from *B. cereus*, and found that when an injection of this was given to guinea-pigs, followed by a large dose of penicillin either immediately or after an interval of up to three days, no penicillin could be detected in the blood at any time. Twenty human subjects were then given 800,000 units of "fortified" procaine penicillin twice daily: after several days a single injection of 800,000 units of penicillinase was given. Penicillin disappeared from the blood within an hour and remained undetectable for 4–7 days despite continued administration as before. Fortunately the enzyme is well absorbed and circulates in active form: it is truly remarkable that it persists in the body for so long. The first clinical trial of this preparation was reported by A. M. Minno and G. M. Davis,[5] of the U.S. Navy: they treated 32 cases of reactions to penicillin consisting chiefly of urticaria and pruritus with or without fever and joint swellings by injecting 1,000,000 units of penicillinase intramuscularly. The patients responded well, but some required a further dose or doses, and all but 12 had had other treatment first: when an antihistamine drug had been used it was continued. A further account of clinical use now comes from Becker himself, who records 46 case reports from physicians in various parts of the U.S.A. who have tried this treat-

[1] Tacking, R., *Acta path. microbiol. scand.*, 1955, **36**, 471.
[2] —— ibid., 1955, **36**, 61.
[3] Markov, W., *Z. Immun.-Forsch.*, 1956, **113**, 253.
[4] Becker, R. M., *New Engl. J. Med.*, 1956, **254**, 952.
[5] Minno, A. M., and Davis, G. M., *J. Amer. med. Ass.*, 1957, **165**, 222.
[6] Becker, R. M., *Ann. intern. Med.*, 1958, **48**, 1228.
[7] Anderson, H. C., *Lancet*, 1954, **2**, 1157.

ment.[6] Different forms of penicillin were responsible for the reactions described, procaine penicillin being mentioned most often: one patient reacted to oral tablets and another, after an interval of ten days, which makes it even more extraordinary, to the penicillin in a dose of poliomyelitis vaccine. Intervals of 9–14 days between administration and the appearance of the reaction were common, and unless benzathine penicillin had been given it seems unlikely that any of the dose could have been left in the body and thus that the enzyme could have exerted its only known effect. Many patients had various other kinds of treatment, but 16 were treated with penicillinase only. All the users seem to have been well satisfied with the results.

Penicillinase obviously cannot act quickly enough to exert any immediate effect in penicillin shock. For other manifestations of sensitivity it apparently has a considerable value, and it should prove particularly useful in reactions to depot preparations, the absorption of which continues for days after the reaction has begun and can progressively exacerbate it. Benzathine penicillin is particularly dangerous in a sensitized patient: the reaction to it in a child described by H. C. Anderson[7] became progressively more severe for several days and could well have ended fatally. In such cases the most effective treatment might well be to cut down on the site of injection and sponge out the remaining drug, but treatment with penicillinase should remove the need for such a drastic measure.

PATIENTS IN MENTAL HOSPITALS

Forty per cent. of the hospital beds of this country are occupied by psychiatric patients. In the face of this situation the problems of treating the mentally ill still receive less attention than they deserve. The administrative and geographical isolation of mental hospitals from general hospitals and hence of psychiatry from general medicine, the stigma attached to mental illness, the lack of specific treatment, and the accumulation of neglected chronic patients continued until well into the present century. Although in all these respects there has been a marked improvement in the last few decades these influences still exist and probably still contribute to the comparative neglect of the psychiatric services which is evident in varying degree throughout the National Health Service. Nevertheless in recent years the desire to improve matters has grown notably stronger. There has been, particularly in Britain, a series of enthusiastic and hopeful therapeutic experiments in mental hospitals, so that after the best part of a century in the doldrums the mental hospital is now again in the forefront of psychiatry. A common factor that has characterized many of these experiments has been the idea of the hospital milieu as a therapeutic force—"a therapeutic community" to use the term which the advocates of this approach have adopted. This viewpoint is implicit also in the report of the Royal Commission on the Law Relating to Mental Illness, which criticized present laws particularly because they impeded such developments and advocated new legislation designed to foster them. The Royal Commission could make no comments upon the administrative, architectural, and professional aspects of psychiatry which, although outside the Commission's terms of reference, probably impede the development of good psychiatric medical care as much as the outmoded nineteenth-century legislation. It may well be that a national inquiry into the mental health services will prove an essential complement to the Commission's inquiry into the law if improved standards of treatment are to be generally achieved. Existing mental hospitals, for example, embody in their architecture an obsolete conception of the psychiatric patient which acts as a positive obstacle to modern treatment. Even so, there is a good deal of doubt about the type of psychiatric hospital that should now be built when the opportunity arises and, indeed, whether new psychiatric hospitals as such should be built at all.

In order to obtain some of the data necessary for a decision on matters such as these the Department of Social Medicine of Birmingham University has recently surveyed the mental hospital population of Birmingham—3,555 patients in all. Reporting their findings, Professor T. McKeown and his colleagues[1 2] stress "the desirability of planning mental hospitals in the light of the most up-to-date information which can be obtained." One finding alone in this survey justifies the emphasis of the Royal Commission on the need for hostels to which psychiatric patients can be admitted on discharge from hospital. The Birmingham workers suggest that 12% of the existing patients could leave the mental hospitals immediately if such accommodation existed, and most medical superintendents in other regions would support this. But there will be less agreement on the significance of some other findings in the survey. Over 30% of the Birmingham patients were said to be "incapable of any work," not even light work on the ward, and over 40% were said to need supervision in "closed blocks." These figures will surprise those who work

[1] Garratt, F. N., Lowe, C. R., and McKeown, T., *Brit. J. prev. Soc. Med.*, 1957, **11**, 165.
[2] —— —— —— ibid., 1958, **12**, 23.

in hospitals which have long adopted an "open-door" policy and an active programme for the rehabilitation of chronic patients. Perhaps such figures tend to reflect the results of long-continued psychiatric practice in hospital buildings that were designed for custody rather than for active treatment and rehabilitation. The fact that 45% of the patients in the survey were said "not to require a regular visit from a doctor" suggests a different view of the psychiatrist's role, and a different attitude to chronic patients, from that which the proponents of the "therapeutic community" have expressed.

The survey's assessment of the mental nurses' function is also unlikely to be accepted by those who believe that mental nursing is something much more than custodial supervision, for the authors state: "We have not included under nursing care the supervision which some patients needed because of their mental state. . . . It seemed better to assess this separately in the discussion of 'supervision' than to confuse it with the requirements for traditional nursing services." This seems to discount the psychotherapeutic element in mental nursing. For planning purposes it is clearly necessary to distinguish the proportion of psychiatric patients who need the laboratory and other facilities and the type of bedside nursing usually associated with a general hospital. As the Birmingham survey shows, the proportion is small, being less than 13%. But the proportion of all patients reported as receiving any form of investigation or active treatment in the mental hospital whether for mental or physical illness was equally small—smaller than the proportion of patients, for instance, who had been in hospital for less than a year: all others received only varying degrees of "maintenance treatment" or "supervision."

The Birmingham survey has provided a useful picture of the mental hospital population of a large city. The proportion of patients who need care similar to that given in a general hospital or of those who remain in mental hospitals for no better reason than that they have nowhere else to go would probably be the same in most parts of Britain. But some of the other figures—for example, the proportion of patients who really need to be accommodated in closed blocks or who are incapable even of light work—would have to be carefully scrutinized before being accepted as a sound basis for planning the full range of accommodation necessary for psychiatric in-patients. Comparative surveys are needed of the situation elsewhere, and particularly as it exists in those mental hospitals which would regard the Birmingham figures as too pessimistic.

HYPOPHYSECTOMY AND DIABETES

The vascular complications of diabetes, especially those affecting the eyes and kidneys, remain the outstanding problem in an otherwise controllable disease. The incidence of complications increases with the duration of the diabetes, and it is perhaps the young diabetic who typifies the serious nature of the problem. The prospect of blindness from retinopathy or retinitis proliferans and of renal insufficiency from intercapillary glomerulosclerosis in early adult life is a gloomy one, especially when so little is known about their aetiology. The risk is greatest in those whose diabetes is subject to wide fluctuations in control, but it is by no means certain that strict adherence to normoglycaemia will prevent their development. It has been suggested that a vascular defect is inherited along with the diabetic tendency, but this seems unlikely in view of reports of typical complications in patients with diabetes following pancreatitis.[1] Another possibility is that some type of hormonal imbalance, affecting particularly the pituitary–adrenal system, is responsible, and this has at least provided a therapeutic approach, albeit a desperate one.

There are several reasons why bilateral adrenalectomy or hypophysectomy might be expected to benefit the patient with severe diabetes. It is well known that removal of these glands will alleviate experimental diabetes. Some of their hormones are insulin antagonists, and adrenal steroids are released in response to stress. It is the diabetic who fluctuates between the stressful conditions of ketosis and hypoglycaemia who is a candidate for complications. Moreover, B. Becker[2] has reported the production of retinopathy in animals by the administration of steroids, though this work has still to be confirmed. Bilateral adrenalectomy has been reported to benefit patients with early complications,[3] but once firmly established the renal disease appears to progress in spite of the operation. The difficulty is to decide when surgery is justifiable. Much interest was aroused by the paper of R. Luft, H. Olivecrona, and their associates[4] on the results of hypophysectomy in 20 patients with severe diabetic complications. Although the operation was technically difficult because of cerebral vascular changes and the mortality high, the degenerative processes did seem to be arrested in some of the patients who survived. It would be interesting to know what has happened in the three years since the paper was published. A few further cases have been reported,[5–8] the largest series being that of E. S. Gordon, who records a "striking" improvement in the retinopathy in all eight patients who survived out of a total of eleven operated upon. It is probable, however, that not all patients have benefited from hypophysectomy, and it would be unwise to infer that this is the treatment

[1] Duncan, L. J. P., MacFarlane, A., and Robson, J. S., *Lancet*, 1958, **1**, 822.
[2] Becker, B., *Ann. intern. Med.*, 1952, **37**, 273.
[3] Malins, J. M., *Lancet*, 1956, **1**, 530.
[4] Luft, R., Olivecrona, H., Ikkos, D., Krarup, T., and Ljunggren, H., *Brit. med. J.*, 1955, **2**, 752.
[5] Kinsell, L. W., Lawrence, L., Balch, H. E., and Weyand, R. D., *Diabetes*, 1954, **3**, 358.
[6] Gordon, E. S., *J. Lab. clin. Med.*, 1956, **48**, 810.
[7] Clinico-pathologic Conference, *Amer. J. Med.*, 1957, **22**, 949.
[8] Slater, J. D. H., and Nabarro, J. D. N., *Proc. roy. Soc. Med.*, 1958, **51**, 365.

of choice for the young diabetic with progressive complications. The diabetes does not necessarily become more stable, nor do insulin requirements always fall. Alternative and safer ways of suppressing pituitary-adrenal function will undoubtedly be found, but the main aim must surely be to establish the reason why an increasing number of diabetics suffer from serious vascular lesions.

A NEW SYNDROME IN ALCOHOLICS

Despite the lack of agreement about the mechanism by which alcohol adversely affects the liver, most physicians would agree that alcoholism is an important factor in hepatic disease, at least in Europe and the U.S.A. Almost everyone is familiar with the malaise and nausea that may follow too enthusiastic an indulgence in alcoholic beverages, and all physicians are acquainted with the diffuse type of cirrhosis that so often attacks the liver of those people who regard alcohol as a main article of diet. Yet a third clinical picture has recently been described which combines certain features of these well-recognized states with others—namely, lipaemia, hypercholesterolaemia, and a moderate degree of haemolytic anaemia.

A series of twenty cases have been collected by L. Zieve at the Minneapolis Veterans Hospital during the past eight years.[1] Many were recognized only retrospectively and were in consequence not studied so comprehensively as the more recent members of the series. But a fairly distinct clinical picture has emerged. The patients were men aged 26 to 65 years of age, and all were heavy drinkers of either beer or spirits. The presenting symptoms were invariably gastro-intestinal, with nausea, vomiting, diarrhoea, and upper abdominal pain, all of some days' or weeks' duration. A low fever was common and loss of weight sometimes striking. Jaundice was present in every patient, the associated findings almost always suggesting that it was of the regurgitant type due to biliary obstruction. Haematological studies, however, revealed that in the majority of these patients a haemolytic process was also at work as shown by a moderate anaemia, increased faecal and urinary urobilinogen, and a raised osmotic fragility of the red cells. To complete the syndrome a conspicuous lipaemia was often present, and a serum cholesterol above 330 mg. per 100 ml. was found on at least one occasion in 19 of the 20 cases. Apart from the evidence indicative of an obstructive type of jaundice there was little clinical indication of hepatic dysfunction. Thus the prothrombin index and the various flocculation tests were usually within normal limits, spider naevi were noted only occasionally, and no patient gave evidence of hepatic encephalopathy. Nevertheless, biopsy of the liver in sixteen cases showed fatty infiltration in fourteen and some degree of cirrhosis in fifteen, ranging from minimal in five to moderate or severe in six.

It is evident that the heavy drinking of alcohol in which all these men indulged before their admission to hospital had led to the form of hepatic injury with fatty infiltration that is now recognized as the common response of the liver to this metabolic insult. Whether it is the result of a direct toxic effect of alcohol on the liver cells,[2] or due to a disturbance of the balance between the lipotropic and alipotropic agents in the diet,[3] is still a moot point, but the fatty livers induced in experimental animals by diets deficient in lipotropic factors are not usually associated with the lipaemia and hypercholesterolaemia that characterize this new syndrome. Nor have haemolytic anaemia and increased osmotic fragility been described in these animals. It is therefore not improbable, as Zieve points out, that the anaemia and lipaemia might be aetiologically related, and he has suggested that a lysolecithin might be produced as a result of the action of a serum lipase on the lipaemic plasma, with consequent haemolysis. Although much work remains to be done to clarify the pathogenesis of this new syndrome, its recognition is important, since its clinical manifestations may be easily confused and patients exposed to unnecessary surgery.

[1] Zieve, L., *Ann. intern. Med.*, 1958, **48**, 471.
[2] Mallov, S., *Proc. Soc. exp. Biol.*, 1955, **88**, 246.
[3] Best, C. H., Hartroft, W. S., Lucas, C. C., and Ridout, J. H., *Brit. med. J.*, 1949, **2**, 1001.

CONTRACEPTION BY INHIBITION OF OVULATION

The Society for the Study of Fertility made a wise choice when it invited Dr. Gregory Pincus, of the Worcester Foundation, Shrewsbury, Massachusetts, to deliver the second Oliver Bird Lecture in London earlier this year, for his investigation of a method of contraception by inhibiting ovulation has aroused much interest. Dr. Pincus entitled his lecture "Fertility Control by Oral Medication." Since animal experiments had shown that progesterone was a potent inhibitor of ovulation and, at certain stages of the cycle, could prevent fertilization and implantation, he had embarked on a clinical study, in collaboration with Dr. John Rock, of its use in preventing ovulation in women. Intramuscular injection, however, had obvious drawbacks, and the oral dose required to prevent ovulation—some 300 mg. daily—was too high for it to be of practical value. Consequently a large series of compounds were investigated in the hope of finding a more active substitute, and certain of the 19-nor steroids proved to be particularly effective. In these, the methyl group in the C-19 position is absent. Three of these compounds are at present being marketed, under the names of "norlutin," "enavid," and "nilevar." All three are potent inhibitors of ovulation, but differ from each other in certain other respects. After extensive animal tests trials were made with enavid in women; these proved its ovulation-inhibiting properties and its harmlessness in other respects. Pincus therefore felt justified in undertaking a field trial of enavid as an oral contraceptive, and this was carried out in Puerto Rico with the collaboration of the local family-planning organization. The number of patients maintained in the trial was 125, defaulters being replaced as required. Each patient took a 10-mg. tablet daily for 20 days from the fifth day of each cycle. Of the original 125 patients,

about half remained at the end of 18 months. Little if any change in their normal menstrual habits was occasioned by the treatment, and various clinico-pathological investigations brought no undesirable effects to light.

The influence of this treatment on the pregnancy rate was remarkable. During a total of 1,279 cycles in which the full course of tablets was taken the pregnancy rate per 100 women years was nil; in 282 cycles in which 1 to 5 tablets were missed out the rate was 9.2; and in 151 cycles in which 5–19 tablets were missed out it was 25.9. These rates compare with a pre-treatment pregnancy incidence of 62.5 per 100 women years; they are all considerably lower than the comparable figures for mechanical methods of contraception. Two years have now elapsed since the trial was begun, and so far no failures have occurred among those who have taken the tablets regularly. In another trial, started in another district and with the benefit of the experience gained in the initial series, less than 1% of the women have defaulted so far, and the method appears to be readily acceptable. These trials constitute a remarkable step forward in the search for a harmless drug which can be taken by mouth to prevent conception. The main drawbacks of the compounds investigated were their considerable expense and the need to take the pills regularly for 20 days in each cycle. With scientists of the calibre of Dr. Pincus taking an interest in this problem, it may not be all that long before the discovery of a cheap contraceptive tablet which will be effective when taken perhaps only once a month.

THE KING'S FUND

The annual report[1] of the King Edward's Hospital Fund for London shows once again how much can still be done for the hospital service by voluntary effort. During the first ten years of the National Health Service the Fund has distributed over £2¼m. to hospitals, convalescent homes, and homes for the aged sick, and its Emergency Bed Service has answered 615,000 requests for admission to hospital and succeeded in securing admission in all but 50,000 of these. The report mentions some of the grants made to individual hospitals during the year: at one hospital, for instance, the money was spent on installing a lift and at another on buying equipment for a geriatric ward—projects for which the hospitals were unable to obtain Exchequer money.

For some time past the Fund has been investigating the causes of "undue" noise in hospital wards. The report states that it is the unnecessary noises made within or near the ward that cause most distress—the squeaking wheel, the heavy footstep, and the slamming door. In an experiment carried out at Paddington Hospital all the patients over a period were asked to send to the Fund a statement on the noises that worried them most. The hospital secretary was then asked if he could eradicate all the causes of noise mentioned. Over the course of several months he succeeded in doing this. Bed screens were stopped from rattling and banging; doors and trolley wheels were oiled and repaired; student nurses were supplied with quiet, comfortable shoes; dressing-trolley tops were covered with a sound-deadening material, and so on. These measures cured much of the noise, but the report states that the noisy patient and, worse, the snoring patient are still unsolved problems. However, with its usual resourcefulness the Fund has some experiments under way to see how this nuisance can be minimized. All who have lain awake in a hospital ward envious of those snoring around them will wish this work well.

[1] King Edward's Hospital Fund for London, *Sixty-first Annual Report, 1957*. London.

LIFE PEERS

Among the first fourteen people to be granted life peerages last week were two medical men—Sir John Stopford, F.R.S., and Dr. Stephen Taylor. For the first time in an honours list it is made known which are the nominees of the Leader of the Opposition, and Dr. Taylor is among the six whose peerage is recommended on his advice.

A Lancastrian born and bred, Sir John Stopford has all his life been associated with Manchester University, where he qualified in medicine in 1911. In 1919 he was made professor of anatomy there (succeeding Sir G. Elliot Smith), and carried out in the department the researches into the neurological basis of sensation that resulted in his being elected a Fellow of the Royal Society at the early age of 39. In helping to expand the University, he proved himself to be a wise guide in its many projects. After serving for a number of years as dean of the medical school and, in 1928–30, as pro-vice-chancellor, he was made vice-chancellor in 1934, in which appointment he remained until retiring in 1956. Acutely conscious of what a university ought to be, and of the unique place it has in Western civilization, Sir John Stopford has never ceased to animate others here and abroad with the same vision. The value of his work in advancing higher education has been immense.

Dr. Stephen Taylor has had a varied career in politics and journalism as well as medicine. During the last war he directed the Social Survey of the Ministry of Information, and then in 1945–50 he was Labour M.P. for Barnet, being for a time Mr. Herbert Morrison's Parliamentary Private Secretary. He was formerly assistant editor of the *Lancet*. At present Dr. Taylor is medical director of the Harlow Industrial Health Service. He has in addition performed much valuable work in his labours to see that the National Health Service runs smoothly. Among these was a survey of general practice carried out under the auspices of the Nuffield Provincial Hospitals Trust, which Dr. Taylor reported in his influential book *Good General Practice*.

Professor A. M. Claye has been re-elected President of the Royal College of Obstetricians and Gynaecologists.

GLUTEN-FREE DIETS

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Following the report of Dicke in 1950 that many children with the coeliac syndrome might be successfully treated with a diet free from wheat and rye flours, it was established that it was wheat and rye gluten which was harmful (Anderson *et al.*, 1952 ; Dicke *et al.*, 1953). Subsequent reports have confirmed the effectiveness of a gluten-free diet in nearly all children with the coeliac syndrome (Ross *et al.*, 1955 ; Sheldon, 1955).

In children with the coeliac syndrome who are intolerant of gluten the enteropathy is thought to be the principal disorder. This is also true in adults with idiopathic steatorrhoea ; and in a proportion of such patients, as well as the children, the withdrawal of gluten from the diet leads to a return of normal intestinal function (Anderson *et al.*, 1954 ; French *et al.*, 1957). It has been suggested (Frazer, 1955) that "gluten-induced enteropathy" might be used as an inclusive term applicable to all patients, regardless of age, in whom a demonstrable enteropathy can be shown to be caused by gluten.

It has not yet been established what level of gluten intake is without effect in a gluten-intolerant individual nor whether there is a dose/response relationship. It seems to be the general experience (Lawson, 1954) that a low level of gluten intake must be maintained for effective therapy, and for these reasons it seems advisable to make a gluten-free regime as complete as possible. Gluten intolerance appears to persist for a long time, and it may be necessary for a gluten-free diet to be continued indefinitely.

There are several kinds of gluten, though all are plant proteins. In medical practice the word "gluten" is usually taken, as in this paper, to refer only to wheat and rye glutens. There is also a gluten in maize, but it seems to be harmless. The amount of protein in oats is low, and its importance in relation to gluten-induced enteropathy has not been finally evaluated. It is not excluded from a gluten-free diet at present, and we have not observed any ill effects from its inclusion. If in the future it appears that oats should be excluded, this could readily be done, because oat flour is rarely used except in porridge, breakfast and baby cereals, and certain cakes.

We here deal only with gluten-free diets and not with other therapy which may be needed, particularly in the early stages of treatment, in gluten-induced enteropathy.

Construction of a Gluten-free Diet

The objective is to provide a pleasant and nutritionally adequate diet without using any food containing even traces of wheat or rye flours. There are two main problems in the construction of such a diet. Firstly, flour is used in so many processed foods that the selection of suitable foods presents difficulties. Secondly, ordinary flour is an important source of protein, calcium, iron, thiamine, and nicotinic acid in the average British diet. This source is lost when gluten-free flour, which is almost pure wheat starch and lacks other nutrients, is used. In practice the nutritional value of a gluten-free diet might be lower still, because the withdrawal of wheat flour also involves removing useful items of cheap protein- and vitamin-containing foods such as fish fried in batter, sausages, and pies. It is difficult to assess the nutritional consequences of the withdrawal of wheat flour from an individual's diet, because there is a wide variation in the intake of flour, depending mainly on personal preference and income group.

With this proviso in mind the data in Table I will serve as a guide. All the nutrients of which flour is a significant source are listed. The figures for the percentage provided by flour are for the population as a whole, and the effects of its exclusion have been calculated, using the levels of intake for adults and children separately.

TABLE I

	Protein	Calcium	Iron	Thiamine	Nicotinic Acid	Riboflavine
Proportion provided by flour in national diet*	29%	24%	27%	31%	26%	7%
	g.	g.	mg.	mg.	mg.	mg.
Adults						
Average daily intake (1954) minus flour†	60·7	0·85	11·0	1·0	10·3	1·7
Recommended daily intake for sedentary man‡	69·0	0·8	12·0	1·0	10·0	1·5
Daily intake from a suitable gluten-free diet (Table II)	76·2	1·25	12·7	1·1	24·0	3·0
Children						
Average daily intake (1954) minus flour†(under 15 years)	28·4	0·5	5·0	0·45	5·75	0·9
Recommended daily intake (7–9 years)‡	68·0	1·0	10·0	0·8	8·0	1·2

* Page 80, *Domestic Food Consumption and Expenditure:* 1954. Annual Report of the National Food Survey Committee. H.M.S.O., London.
† Page 62, ibid.
‡ Page 45, *Manual of Nutrition*, published by the Scientific Advisers' Division (Food) of the Ministry of Agriculture, Fisheries, and Food, 1955. H.M.S.O., London. (Based on recommendation, British Medical Association, 1950.)

The recommended levels of intake are shown and also the actual intake provided by a suitable gluten-free diet (Table II) in which alternatives to gluten-containing foods have been used. It will be seen that the removal of flour from the adult dietary reduces the intake of protein to below that recommended and the intake of other nutrients to near the recommended level. In the child, the intakes of all the nutrients listed are reduced well below the recommended levels because the national levels of intake are already marginal. It follows, therefore, that in constructing a gluten-free diet, not only must attention be directed towards excluding all gluten-containing foods but care must also be taken to see that the diet contains adequate calories, protein, calcium, iron, thiamine, and nicotinic acid, which may otherwise be deficient, particularly for a child.

In Table II are listed quantities of different foods which might be eaten by an adult as one day's gluten-free diet. They yield 2,500 calories (sufficient for a man in sedentary work) and other constituents as shown in Table I. Such a diet is also nutritionally adequate in other respects. About 20% of the iron, thiamine, and riboflavine in this diet is

TABLE II.—*A Possible Single Day's Gluten-free Diet for an Adult*

	Grammes	Homely Measures
Bacon	40	One rasher
Cabbage (cooked)	50	One tablespoonful
Cheese	40	One and a half ounces
Cornflakes	30	Three tablespoonfuls
Gluten-free flour	140	Five ounces
Honey	15	One teaspoonful
Lettuce	20	Four leaves
Margarine	30	One ounce
Marmalade	15	One teaspoonful
Meat	100	One medium steak or chop
Milk	600	One pint
Potatoes	120	Four medium ones
Rice (dry)	20	Three teaspoonfuls
Sardines	30	Three
Sugar	40	Six teaspoonfuls
Tomatoes	100	Two medium ones
Yeast	15	One dessertspoonful

provided by yeast, and if for any reason the patient does not eat gluten-free bread (which usually incorporates the yeast) an adjustment should be made. The yeast can be taken as a drink with fruit juice or replaced by an additional egg plus half a pint (280 ml.) of milk. In the child greater care is needed, as is evident from Table I. Particular emphasis should be placed on a high consumption of milk and dairy products. If the child's appetite is poor, calcium, iron, and vitamin B complex supplements should be given.

Tables III, IV, and V have been found useful when advising patients what foods may or may not be eaten. In Appendix 1 are given alternative foods for different meals, and in Appendix 2 recipes using gluten-free flour for popular foods which would otherwise be excluded from a gluten-free diet.

TABLE III.—*Foods Forbidden in a Gluten-free Diet*

As a general rule, *any* processed, prepared, or tinned food must be assumed to contain gluten unless definite information is available to the contrary.

Baking powders
* Baby cereals ("farex," "robrex," etc.)
* Beans, baked, canned
Bemax
Bengers food
Biscuits
* Blancmange powders
Bread
Breadcrumbs
* Breakfast cereals
Buns
Cake and pudding mixes
Cakes
Cake decorations
* Canned meats
* Caramels
* Celery salt
* Cheese spreads
* Chocolate
* Chocolate, drinking
Chocolate and coffee spreads
Christmas puddings
* Chutney
* Coffee essences
* Cornflour
Cream, artificial
Crispbread
* Curry powder
* Custard powder
Dessert powders
Energen rolls
Energen bread
Farola
Farinoca
Farley's rusks
* Fish canned in sauce
* Fish pastes
Glacé fruits
Golden raising powder
* Gravy makers and browning
* Groats
Horlicks
Horseradish sauce
* Ice cream
Ice-cream cones and wafers
Ice-cream powder
* Infant and invalid foods
* Instant desserts
* Junket preparation in tablets
* Lemonade powder
Lemon cheese
Lemon/orange curd
Lemon-pie fillings
Luncheon meats
Macaroni cheese
Macaroni products
Macvita
* Malt
Malted milk drinks
Marshmallow creme
Marzipan
* Mayonnaise
* Meat-pastes
* Meat, canned
* Meringues
Mincemeat
Mustard
* Oatmeal
Ovaltine
* Oxo
Pastry
Peanut butter
* Pepper
Pies
* Pickles in sauce
* Porridge oats
* Potato crisps
* Potato salad
Puddings, canned
Ryvita
* Salad dressings
* Sandwich spreads and pastes
Sardines in sauce
* Sauces
Sausages
Semolina
* Soups, canned
Soup powder
Spaghetti
* Spices
* Spreads
Stuffings
Tomatoes in sauce
* Tomato juice
Trifle
* Vegetable salad
Vegetables canned in sauce
Vermicelli
Vitawheat

* Foods marked with an asterisk are sometimes available in a gluten-free form, and appear in Table V.

TABLE IV.—*Foods Which Are Acceptable*

Almonds
Bacon
Beer
Bicarbonate of soda
Bovril
Boiled sweets (clear only)
Butter
Calves-foot jelly
Capers
Carraway seeds
Cheese
Chicory
Cloves
Cocoa
Coconut
Coffee (fresh or instant)
Colourings
Cooking-fat
Cooking-oil
Cream, dairy or tinned
Cream of tartar
Dried fruits, all kinds
Eggs
Essences
* Fish, fresh, all kinds
Fish canned in brine, oil or water
* Fruit, fresh, all kinds
Fruit juices and squashes
Fruit tinned in syrup
Gelatin
Ginger
Glucose
† Gluten-free flour
Herbs
Honey
Jam
Jam setters
Jelly (crystals, cubes, etc.)
Junket (rennet)
Lard
Lemon juice
Lemonade (bottled) and aerated waters
Lentils
Lime juice
Margarine
Marmalade
Marmite
* Meat, fresh, all kinds
Milk, fresh
Milk, tinned or dried
Olives
Peels
Pickles, clear
Prunes
Raisins
Rice
Sago
Salt
Suet
Sugar
Sultanas
Table waters
Tapioca
Tea
Treacle (golden syrup or molasses)
* Vegetables, fresh or dried, all kinds
Vegetables canned in brine or water, all kinds
Vinegar
Wines and spirits
Yeast, bakers'

* Frozen foods, provided they are not already prepared in any way, may be used instead of fresh.
† For supply and uses, see below.

Gluten-free Flour

Gluten-free flour (that is, wheat flour from which all gluten has been removed) may be obtained in 7-lb. tins (7s. plus postage) from Energen Foods Ltd., Pound Lane, Willesden, London, N.W.10.

Bread made from gluten-free flour and yeast may be obtained by post from Birkett and Bostock Ltd., Dept. T.R.D., Coronation Bakery, Stockport, Cheshire, cost (1957) 1s. 3d. per 12-oz. loaf, plus postage. This firm also supplies wheat starch, gluten-free rusks, sweet biscuits, shortcake, and "Tendercake Dry-Mix" (price, 1957, 1s. 6d. per lb.). The latter contains all the ingredients, except water, for gluten-free bread; instructions are enclosed.

Local bakeries will sometimes bake gluten-free bread if there is a sufficient and regular demand, but most patients prefer to bake their own.

TABLE V

The following manufacturers have assured us that their products listed below are gluten-free. Only a selection of firms have been contacted, and doubtless others would be equally co-operative if approached. Some of these manufacturers also market gluten-free foods listed in Table IV.

Alfred Bird and Sons Ltd.: Blancmange powder. Custard powder. Instant postum. Instant whip. Rice toasties.
Brown and Polson Ltd.: Cornflour.
Cadbury Bros. Ltd.: All products at present except biscuits.
Cerebos Ltd. (Saxa): Bisto. Pepper. Spices.
Chocolate Tobler Ltd.: Toblerone and all assorted packs and bars.
Crosse and Blackwell Ltd.: Baked beans. Browning. Celery salt. Chef tomato ketchup. Fulcreem custard powder. Herring in tomato. Mayonnaise. Rennet essence. Salad cream. Sandwich spread. Sweet mango chutney. Sweet mixed pickles. Tomato ketchup.
Fray Bentos (Oxo) Ltd.: Beef: pressed, rolled, and brisket. Chicken breasts in aspic. Corned beef. Crab. Cream of tomato soup. Lemco. Minced chicken. Ox tongues.
J. S. Fry and Sons Ltd.: All products at present except "Tiffin."
H. J. Green and Co. Ltd.: Blancmange powder. Carmelle. Complete custard mix. Cornflour. Custard powder. Gravy salt. Lemonade powder.
H. J. Heinz and Co. Ltd.: Celery salt. Chutney. Gravy browning. Ideal sauce. Junior fruit dessert and pineapple. Mayonnaise. Piccalilli. Pickle: Ideal, Mixed, Royal. Potato salad. Salad cream. Sandwich spread. Soups: cream of asparagus, cream of celery, cream of green pea, cream of onion, cream of spinach, cream of tomato. Strained: apples, apricots with rice, beetroot, carrots, rice pudding. Kipper spread. Chocolate pudding, cream cereal, egg custard with rice, green beans, peas, pineapples with rice. Tomato juice. Tomato ketchup. Vegetable salad. Worcestershire sauce.
H.P. Sauce Ltd.: H.P. baked beans. H.P. pickle. H.P. salad cream. H.P. tomato ketchup. H.P. tomato soup.
Keen Robinson and Co. Ltd.: Robinson's patent barley and patent groats. Ready-cooked groats and baby rice. Robsoup—chicken and bone and vegetable varieties. Three Bears oats.
James Keiller and Son Ltd.: All chocolate and sweet packs.
Kellogg and Co. Ltd.: Corn flakes. Rice krispies. Sugar-frosted flakes. Sugar ricicles.
Kraft Foods Ltd.: Processed cheeses, all varieties at present. Caramels. Mayonnaise. Miracle whip. Salad cream. Salad dressing. Tomato chutney. Tomato ketchup.
J. Lyons and Co. Ltd.: Bev. Boiled sweets. Chico. Chocolate, all varieties. Custard powder. Meringues. Mousse, all flavours. Ready Brek. Strawberries in melba sauce.
Nestlé Coy. Ltd.: Chocolate—all varieties *except* cracker milk bars, crispette biscuit centres, and turkish delight chocolates. Lactogen. Milo chocolate food drink. Nesquik instant chocolate. Swiss Knight petit gruyère cheese.
Quaker Oats Ltd.: Oat krunchies. Quaker one-minute oats.
Rowntree and Co. Ltd.: Aero. Beechnut chewing-gum. Elect cocoa. Fruit gums. Fruit pastilles. Milk motoring chocolate. Polo fruits. Polo mints. Sunchoc.
A. R. Scott Ltd.: Scott's porage oats. Piper oatmeal. Scott's baby cereals: M.O.F., ready-cooked groats.
Smith's Potato Crisps Ltd.: Potato crisps.
A. Wander Ltd.: Vimaltol.
Ice cream: J. Lyons and Co. Ltd.—all varieties *except* Wonder Ice Cake. Midland Counties Dairies Ltd. Tudor Dairies Ltd., Henley. T. Wall and Sons Ltd.—all varieties except Gaycakes.

Summary

It is now widely held that most children with the coeliac syndrome and many adults with idiopathic steatorrhoea are intolerant of gluten and are much improved by a gluten-free diet. Such a diet may lack essential nutrients unless care is taken in its construction; milk and yeast are particularly useful in providing the protein, calcium, iron, thiamine, and nicotinic acid which is lost when flour is removed from the average British diet. With so many processed foods now available it is difficult to know which may be used. Lists of gluten-containing and gluten-free foods are given.

We thank Professor A. C. Frazer for encouragement and advice and the food manufacturers who so readily supplied information about their products. This publication is part of the research programme of the Department of Medical Biochemistry and Pharmacology of the University of Birmingham, which is partly financed by a grant from the Medical Research Council, to whom we are much indebted.

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APPENDIX 1

The following are suggested alternatives for different meals of a gluten-free diet:

Breakfast.—Porridge. Cornflakes. Rice krispies. Puffed rice. Oat krispies. Egg, boiled, poached, scrambled, or fried. Bacon, grilled or fried. Kippers. Smoked haddock, poached in milk or water. Kedgeree (flaked boiled fish, boiled rice, chopped egg, salt). Gluten-free bread or biscuit. Butter or margarine. Marmalade or preserves. Tea or coffee with milk and/or sugar.

Lunch.—Soups—bone stock. Any variety of vegetable. Marmite or bovril can be used. To thicken add pearl barley, split peas, or gluten-free flour. Any type of fresh meat, roasted, grilled, fried, or braised. Stew (thicken with gluten-free flour). Tripe. Liver. Kidney. Heart. Fish, boiled, steamed, or grilled (if fried, dip in egg, then in gluten-free flour to coat). Fish in egg custard (egg and milk). Cold ham. Any variety of fresh vegetable. If white sauce is made, thicken with gluten-free flour. Gravy—natural juice of meat, thicken with gluten-free flour. Fruit, fresh or tinned. Sago or rice pudding. Custard (use recommended custard powder only). Jam tart (pastry made with gluten-free flour). Jelly, ice cream (recommended varieties). Blancmange and fruit (recommended custard powder). Sponge cake and custard (see recipe).

High Tea or Supper.—Omelettes. Bacon. Egg. Mushrooms. Soused herrings and salad. Sardines in oil and salad. Toasted gluten-free bread with grated cheese. Gluten-free bread. Butter or margarine. Jam or preserves. Cakes (as recipes). Biscuits (as recipes). Puddings as for lunch.

Bedtime Drinks.—Milk. Cocoa (recommended varieties). Fruit juice. Tea or coffee with milk and/or sugar.

APPENDIX 2

Gluten-free flour is used in the following recipes:

1. YEAST LOAF

12 oz. (340 g.) gluten-free flour.
12 oz. (340 ml.) lukewarm water and milk mixed.
1 oz. (30 g.) yeast started with 1 teaspoonful sugar.
½ oz. (15 g.) cooking fat.
1 teaspoonful salt.

Add the salt to the gluten-free flour and rub in the fat. Mix the creamed yeast and sugar with the milk and water, and stir into the gluten-free flour thoroughly, seeing that no lumps are left. Allow the mixture to stand in a warm place for 20 minutes exactly. Pour the batter into two 1-lb. (two 450-g.) size bread tins, previously warmed and greased. Bake at Regulo 3 (320° F.) for 20 minutes, then turn up the gas to Regulo 7 (400° F.). Leave for 10 minutes. Take the loaves out of the tins, turn upside down on the oven shelf, and continue cooking for 15 more minutes.

2. SWEET LOAF

½ lb. (230 g.) gluten-free flour.
1½ oz. (45 g.) sugar.
2 oz. (60 g.) margarine.
3 teaspoonfuls gluten-free baking powder (Recipe No. 9).
4 oz. (115 ml.) milk.
½ teaspoonful salt.

Sieve dry ingredients. Rub in margarine, then make a well in the centre and mix in enough milk to make a soft dough. Mix quickly and lightly and turn the dough into a well-greased shallow tin. Bake for 30 minutes at Regulo 7 (400° F.). When cool, cut into slices and serve with butter or margarine.

3. WHEAT STARCH CAKE

½ lb. (230 g.) gluten-free flour.
4 oz. (115 g.) sugar.
4 oz. (115 g.) margarine.
1 teaspoonful salt.
3 teaspoonfuls baking powder.
4 oz. (115 ml.) milk.
1 egg—optional.
Flavour with coconut, dates or cocoa.

Sieve the dry ingredients into a basin, rub in the margarine, then make a well in the centre and mix in enough milk to make a soft dough. Mix quickly and lightly and turn the dough into a well-greased shallow tin. Bake for about 30 minutes at Regulo 7 (400° F.).

4. WHEAT STARCH BISCUITS

4 oz. (115 g.) margarine.
4 oz. (115 g.) sugar.
3 oz. (85 g.) gluten-free flour.
3 oz. (85 g.) ground rice.
1 egg.

Cream margarine and sugar, add beaten egg, gluten-free flour, ground rice. Mix to dough. Roll out thinly, prick all over and cut into shapes. Place on a greased tin. Bake for 15 minutes at Regulo 3 (320° F.). This mixture will make 1 lb. (450 g.) of biscuits.

5. SWISS ROLL

4 eggs.
4 oz. (115 g.) sugar.
2 oz. (60 g.) gluten-free flour.
2 oz. (60 g.) ground rice.

Beat eggs and sugar over hot water until light and fluffy. Fold in sieved gluten-free flour and ground rice; pour mixture in lined swiss-roll tin. Bake at Regulo 8 (450° F.) for 7 to 10 minutes.

6. CORNFLOUR CAKE

4 oz. (115 g.) cornflour.
1 level teaspoonful baking powder.
2 oz. (60 g.) butter.
3 oz. (85 g.) castor sugar.
2 eggs.
Grated rind of 1 lemon.

Sieve the cornflour and baking powder together; cream the butter and sugar very thoroughly. Add the well-beaten eggs, then the cornflour and grated lemon rind. Beat all well together. Put into a well-greased tin and bake for about 30 minutes at Regulo 4 (360° F.).

7. PASTRY, SHORT CRUST

4 oz. (115 g.) gluten-free flour.
2 oz. (60 g.) margarine.
2 oz. (60 ml.) water.

Normal short-crust pastry method. Bake at Regulo 7 (400° F.) for 25 minutes. This pastry is not suitable for pies.

8. YORKSHIRE PUDDING

1 egg.
2 oz. (60 g.) gluten-free flour.
5 oz. (140 ml.) milk.
Salt.
Pepper.

Method as for Yorkshire pudding.

9. SPECIAL GLUTEN-FREE BAKING POWDER

3 oz. (85 g.) cornflour.
3½ oz. (100 g.) bicarbonate of soda.
2 oz. (60 g.) cream of tartar.
2 oz. (60 g.) tartaric acid.

Mix all ingredients together and rub through a hair sieve. Repeat twice, then store in an airtight tin.

ANAEMIA AND THE ALIMENTARY TRACT

CONFERENCE AT ROYAL COLLEGE OF PHYSICIANS

[FROM A SPECIAL CORRESPONDENT]

The Royal College of Physicians of London launched a new and highly successful venture last week-end. This was a postgraduate conference on "Anaemia and the Alimentary Tract"—the first of a series which the College intends to arrange. The conference, which was held on July 25 and 26, was attended by 117 physicians and pathologists, and 20 papers by leading workers in this field were read and discussed. The President of the College, Professor ROBERT PLATT, explained that the purpose of these conferences would be to enable fellows and members of the College to hear about recent advances in certain specific branches of medicine.

Lesions of the Mouth and Oesophagus

Dr. R. ASHER (London) began by describing the lesions which might affect the mouth and throat in anaemia. The

mouth and throat were the only parts of the alimentary tract which could be examined without instrumentation. It was merely necessary to ask the patient to open his mouth and say "Ah." A smooth tongue might be found in pernicious anaemia or in patients with iron deficiency, and there might be characteristic changes in the gums in certain types of leukaemia. Pallor of the tongue was a useful diagnostic sign of anaemia in coloured people. In the malabsorption syndrome the state of the tongue might be a sensitive index of intestinal function.

Dr. W. SIRCUS (Edinburgh) estimated that approximately one in five of the general population suffered from aphthous stomatitis at some time in their lives. The lesions might be single or multiple, and recurrences were frequent. In many patients there was anxiety or mental stress, and in others malabsorption might be a predisposing factor. The term Behcet's syndrome was best reserved for those who developed genital and ocular lesions in addition. The mainstay of treatment was local hydrocortisone, but parenteral steroid therapy might sometimes be necessary.

Dr. T. D. KELLOCK (London) discussed the oesophageal lesions which might be produced by anaemia. Long-standing iron deficiency might be followed by the development of a postcricoid web causing dysphagia (the Plummer–Vinson or Patterson–Kelly syndrome). This syndrome could be diagnosed best radiologically, and it was important to recognize that it might be a precancerous condition. However, oesophageal conditions themselves could produce anaemia. The anaemia was usually due to blood loss from such lesions as hiatus hernia, carcinoma, diverticulum, or varices.

Histological and Cytological Appearances

Professor H. A. MAGNUS (London) described the morbid anatomy of the stomach in anaemia. In 17 patients with pernicious anaemia whose stomachs had been examined with the help of Dr. C. C. Ungley, there was atrophy of the body mucosa and thinning of the muscle coats of the stomach. Recent work using the flexible gastric biopsy tube designed by Wood had revealed that both atrophic gastritis and gastric atrophy might be found in pernicious anaemia. Furthermore, the lesion of the stomach in pernicious anaemia was not specific, for gastric atrophy might be found in other conditions. In some patients a few surviving parietal cells might be seen in biopsy specimens, and in the case of juvenile pernicious anaemia described by Mollin and his colleagues the gastric mucosa had appeared histologically normal. In this rare type of pernicious anaemia free acid was found in the gastric juice.

Dr. MARGOT SHINER (London) reported her experience using gastric and intestinal biopsy tubes. The techniques were relatively simple and could be carried out on out-patients. Haematemesis had been an infrequent complication of gastric biopsy, and melaena had been noted in only two of more than 150 intestinal biopsies. Her most striking observations had been made in patients with the malabsorption syndrome. In idiopathic steatorrhoea there was invariably marked atrophy of the villi of the small intestine, and this was not reversible by treatment. She had had similar observations in a child with coeliac disease. In contrast, intestinal biopsies were usually normal in patients with pancreatic steatorrhoea, post-gastrectomy steatorrhoea, or regional ileitis. Gastric biopsies were often normal in idiopathic steatorrhoea, although atrophic gastritis had occasionally been found. In pernicious anaemia the situation was reversed, for gastric biopsies were invariably abnormal and intestinal biopsies were normal.

Dr. R. O. K. SCHADE (Newcastle) emphasized the importance of exfoliative cytology in the early diagnosis of gastric carcinoma. From a study of gastric washings he had been able to make a correct diagnosis in 30 patients in whom clinical, radiological, and gastroscopic examinations had failed. However, Mr. A. W. KAY (Glasgow) thought cytological evidence was not altogether reliable: he had seen two false positives.

Test Meals

Dr. K. B. TAYLOR (Oxford) discussed the use of "diagnex" tests and uropepsin measurements in the study of gastric secretion. Diagnex tests had the advantage over standard test meals that they dispensed with the need for intubation. However, these tests were not infallible, for falsely negative results might be obtained, and they were qualitative rather than quantitative. The measurement of uropepsinogen in urine had been found useful in studying gastric function in patients with pernicious anaemia, in iron-deficiency anaemia, and after gastrectomy.

Mr. A. W. KAY (Glasgow) gave a lucid account of the pharmacological basis for the augmented histamine test. Antihistamine drugs given parenterally were known to antagonize the effects of histamine without affecting its gastric secretory action. Following an intramuscular injection of an antihistamine it was therefore possible to study the effect of large doses of histamine on gastric secretion. He had found that the amount of histamine required to produce maximal gastric hydrochloric secretion was 0.04 mg. per kilogram of body weight. The effect of this injection was most marked between 15 and 45 minutes afterwards. The test gave a measure of the maximal secretory capacity of the stomach and had proved useful in the study of patients with peptic ulcer as well as in the diagnosis of pernicious anaemia.

Newer Techniques for Investigating Anaemia

Dr. SHEILA CALLENDER (Oxford) pointed out the value of measuring the serum iron in iron-deficiency anaemia and in controlling therapy in haemochromatosis. Studies of the absorption of iron were best done using a radioactive iron. She recommended using a faecal-excretion technique, as measurement of plasma radioactive-iron curves of red-cell uptake after oral doses, although simpler, was less satisfactory. Dr. Callender emphasized that the absorption of inorganic radioactive iron might not reflect the capacity of the intestine to absorb food iron. This difficulty had been overcome by the preparation of foodstuffs labelled with radioactive iron, and studies had shown that the absorption of iron from different foodstuffs might be variable.

Dr. D. L. MOLLIN (London) described the use of assays of the serum vitamin B_{12} and of radioactive vitamin B_{12} in the investigation of the megaloblastic anaemias. B_{12} deficiency was best diagnosed by measuring the B_{12} concentration of serum using *Euglena gracilis*. Patients with pernicious anaemia invariably had lower levels of B_{12} in the serum than normal subjects, and in subacute combined degeneration of the cord the B_{12} concentrations were extremely low irrespective of the degree of anaemia. Low serum-B_{12} concentrations were also found in patients who had developed megaloblastic anaemia following gastrectomy and in the blind-loop syndrome. About half the patients with idiopathic steatorrhoea had subnormal B_{12} levels. The absorption of vitamin B_{12} could be measured using radioactive vitamin B_{12}. Patients with pernicious anaemia absorbed subnormal amounts of a test dose of radioactive B_{12}, but this absorption defect could be corrected by intrinsic factor. In contrast, intrinsic factor did not improve absorption of B_{12} in patients with the intestinal malabsorption syndrome.

Professor J. V. DACIE and Dr. I. CHANARIN (London) reported investigations of the metabolism of folic acid. Unlike vitamin B_{12}, folic acid could not be detected in serum under normal conditions, and folic acid deficiency must therefore be diagnosed by indirect means. A "folic acid clearance test" had been found useful for this purpose. The clearance of folic acid from the plasma was studied after the intravenous injection of a small amount of folic acid. In patients with folic acid deficiency associated with the malabsorption syndrome, the clearance of folic acid was very much more rapid than in normal subjects. There was a similar rapid clearance in some patients with pernicious anaemia. The absorption of folic acid had been studied by measuring the serum concentration of folic acid

after a standard oral dose: absorption was usually abnormal in patients with idiopathic steatorrhoea, but might return to normal after a period of treatment with a gluten-free diet.

Steatorrhoea

Dr. W. P. H. SHELDON (London) described the clinical features of coeliac disease in children. Anaemia was usually microcytic, but occasionally a megaloblastic anaemia responding to folic acid might occur. In some children symptoms were mild or absent and the only clinical feature might be lack of growth or irritability. Treatment with a gluten-free diet caused a remission of symptoms and clinical improvement. How long the restricted diet should continue varied in different cases. Out of 95 cases he had found that 72 were able to return to a normal diet eventually. Of the 23 children who relapsed when they tried the normal diet, 11 showed a return of symptoms, but in 12 the only evidence of relapse was lack of growth. Dr. Sheldon therefore stressed the importance of accurate weight and height charts in the management of this condition.

Dr. W. T. COOKE (Birmingham) pointed out that the term "adult steatorrhoea" embraced a variety of conditions such as biliary obstruction, pancreatic dysfunction, regional ileitis, resection of the stomach or bowel, tropical sprue, and adult coeliac disease (idiopathic steatorrhoea), which shared the common feature of an excess excretion of fat in the stools. Symptoms were not usually diagnostic, and neither radiological nor chemical studies of stool fat or nitrogen were satisfactory in distinguishing between them. Anaemia was a constant feature of adult coeliac disease and might be due to deficiency of iron, vitamin B_{12}, or folic acid.

Dr. J. BADENOCH (Oxford) reviewed the history of macrocytic anaemia in association with intestinal lesions. It had been found that stagnation of intestinal contents in blind loops associated with anastomosis or stricture of the intestine might lead to macrocytic anaemia. In 1954 he and Dr. P. D. Bedford had reported that a similar syndrome might develop in patients with multiple diverticula of the small intestine. These patients were unable to absorb B_{12} normally, although absorption became normal after a course of chlortetracycline: it appeared that bacteria interfered with their absorption of vitamin B_{12}. Steatorrhoea occurred in one-fifth of patients with the blind-loop syndrome, and neurological lesions and subacute combined degeneration of the cord might develop. Anaemia was usually macrocytic and megaloblastic, but was sometimes due to blood loss. In diagnosis, Dr. Badenoch stressed the importance of careful radiological studies. Treatment consisted in the administration of B_{12} and folic acid for the anaemia, together with calcium and a wide range of other vitamins.

Treatment of Patients

Dr. P. B. B. GATENBY (Dublin) stressed the importance of assessing the efficacy of the many iron preparations available for treating iron-deficiency anaemia. In a careful study of anaemia in pregnancy, he had found that ferrous gluconate was the most satisfactory oral preparation. Intolerance to oral iron had been the commonest indication for parenteral treatment; malabsorption was another.

Dr. A. S. DOUGLAS spoke on behalf of Professor L. J. DAVIS (Glasgow). The treatment of megaloblastic anaemia was largely the treatment of pernicious anaemia, and for this he recommended an initial injection of 1,000 μg. vitamin B_{12}, followed by 250 μg. weekly. A single injection of 250 μg. monthly was sufficient for maintenance therapy. In the treatment of subacute combined degeneration of the cord more frequent injections were necessary. Folic acid was usually required in treating patients with steatorrhoea, with or without vitamin B_{12}, and in megaloblastic anaemia of pregnancy folic acid should be used. Occasionally megaloblastic anaemia might occur in a patient with scurvy, and this responded to ascorbic acid.

Dr. C. F. HAWKINS (Birmingham) was in favour of a special treatment clinic for patients with steatorrhoea. In their management, electrolyte deficiencies and anaemia should be treated as they arose. Steroid therapy caused only temporary remission in idiopathic steatorrhoea, and he recommended treatment with a gluten-free diet in all cases. Such treatment was highly successful. Failure usually meant wrong diagnosis, a diet not completely gluten-free, or too short a period of dietary treatment. Dr. N. COGHILL (London) asked whether treatment with gluten-free diet could ever be stopped in adults. In his opinion there was a definite risk of cirrhosis of the liver developing in patients with steatorrhoea. Dr. HAWKINS thought that adult patients with idiopathic steatorrhoea should be treated with a gluten-free diet permanently and he agreed that there was a risk of cirrhosis in these patients. However, Dr. W. T. COOKE had seen 25 patients with adult coeliac disease at necropsy, and in only one, an elderly patient of over 70, was there evidence of hepatic fibrosis.

Bleeding from the Alimentary Tract

Dr. G. DISCOMBE (London) discussed the occult blood test. He considered that orthotolidine tests were more satisfactory than those employing benzidine. He had also been developing a screening test. It required a fresh specimen of stool, which was simply mixed with the reagent. The test was useful in detecting bleeding in patients who had been taking aspirin or in those whose bleeding was spasmodic.

Professor L. J. WITTS (Oxford) described the anaemia which may occur after gastric operations. The commonest type of anaemia was due to iron deficiency. Its cause was uncertain. Studies with radioactive iron had shown that absorption was usually normal. Episodic bleeding might play a part in the development of iron deficiency, and if anaemia were severe bleeding should always be suspected. Treatment consisted in the administration of oral or parenteral iron. In some patients there was atrophy of the gastric remnant after partial gastrectomy, and B_{12} deficiency and megaloblastic anaemia might develop. Patients after total gastrectomy had lost their entire intrinsic-factor-secreting area and therefore invariably developed vitamin-B_{12} deficiency and megaloblastic anaemia if they survived long enough to exhaust their body stores. Such patients therefore should either be kept under close haematological supervision or be treated with prophylactic injections of vitamin B_{12}.

Dr. F. AVERY JONES (London) reviewed his experience of unexplained alimentary bleeding. Among 2,526 cases of bleeding from the upper alimentary tract there had been no radiological abnormality in 720 cases. Early gastroscopy had been performed, and in one-third of these latter cases acute ulcers were found, usually on the posterior wall or lesser curvature of the stomach. The prognosis in women with this condition was reasonably good, but men were more liable to develop a chronic gastric ulcer requiring operation at a later stage. Other causes of haematemesis were acute erosive gastritis, oesophagitis, the Mallory–Weiss syndrome, and the taking of aspirin, which might play a significant part in both ulcer patients and those with acute lesions.

In the discussion Professor G. M. WILSON said he thought that dietary iron might not be so readily absorbed by post-gastrectomy patients who became anaemic as by normal persons.

Conclusion

The final session of the conference took the form of a general discussion on anaemia and the alimentary tract under Professor PLATT'S chairmanship. Dr. W. T. COOKE, Professor J. V. DACIE, Dr. F. AVERY JONES, Dr. G. DISCOMBE, and Professor L. J. WITTS took part.

This conference, the first of its kind to be arranged by the College, was an outstanding success. The high standard of the papers was matched only by the excellent organization throughout. No speaker was allowed to exceed his allotted time, and the programme at no time fell behind schedule. Other agreeable features were the dinner given by the College and the buffet meals taken in the Library under the watchful eyes of William Harvey.

British Medical Association

ANNUAL MEETING, BIRMINGHAM, 1958

SUMMARY OF PROCEEDINGS

THE SECTIONS

SECTIONS OF SURGERY, ACCIDENT SURGERY, AND ORTHOPAEDICS

Thursday, July 17

Treatment of Accidents in Small Communities

Mr. H. J. SEDDON (London), president of the Section of Orthopaedics, took the chair when the combined Sections of Surgery, Accident Surgery, and Orthopaedics considered the treatment of accidents in small communities. Sir HARRY PLATT (Manchester), in opening the discussion, reminded his audience of the lessons learned from Sir Robert Jones during the first world war, and of the further lessons learned in the second world war and Korean war. The inter-war years saw the establishment of fracture clinics and of special accident hospitals, and now at many hospitals throughout the country there were accident centres serving populations of 50,000 to 100,000. It should be possible for these centres to cope with a disaster such as a major train accident, sending out mobile teams if required, but they needed the assistance of the local general practitioner at the scene of the accident. In the periphery round the accident centres were the cottage hospitals, and it was here also that the general practitioner had an important role, but these hospitals should not be autonomous but integrated with the main hospital in the group. Sir Harry Platt suggested that all potential surgeons, whether training for general surgery or a specialty, should have a thorough training in accident work.

Professor F. A. R. STAMMERS (Birmingham) also recalled the experience gained in wartime, particularly of resuscitation and adequate replacement of blood lost in accidents. He pointed out that it was impossible either to provide full major hospital services for every accident case or to transfer all such cases to a large general or accident hospital. The patient with multiple serious injuries had to be transferred after appropriate resuscitation had been started, but the minor injury should be treated in the local hospital. Professor Stammers compared this arrangement with the base and forward hospitals of the Army, dealing respectively with major and minor trauma.

Mr. W. C. GISSANE (Birmingham) mentioned that accidents were the main cause of deaths before the age of 35, and compared the treatment of accidents in small communities with that required on a battlefield. Co-ordination between the battlefront and base hospital was essential, and it was equally important between the civilian peripheral hospital and the accident centre. At the periphery the first step was to prevent irreversible shock by ensuring an adequate airway and by blood transfusion. The second step was the diagnosis and repair of injuries, the patient being transported to the main hospital while resuscitation was maintained.

Mr. Gissane suggested that there should be a central accident hospital in each region. These hospitals should be adjacent to a general hospital, and would have mobile teams to send out to the small peripheral hospitals. Surgical training would also be undertaken at these central accident hospitals.

Mr. W. S. LEWIN (Oxford) dealt with the management of head injuries, and pointed out that they were found in 75% of fatal road accidents and that frequently there were injuries to other parts of the body. However, three-quarters of all head injuries were uncomplicated and did not require neurosurgical treatment; they therefore were no problem in a small isolated community. There should be one hospital in each area to provide an efficient 24-hour neurosurgical service, but it was essential that there should also be good transport between the periphery and this main hospital. At the main hospital postgraduate training would be given, and consultants would visit accident cases in peripheral hospitals.

Mr. T. G. LOWDEN (Sunderland) spoke about the multiplicity of hospitals in some towns, each dealing with its own particular type of emergency—for example, general surgical, medical, eyes, etc. He suggested therefore that the "collecting system" of patients should be simplified. There were many accident cases, of a minor nature, which could be treated efficiently at a smaller peripheral hospital, and as examples the large number of minor head injuries and burns were given. By this means the patients would be saved long and unnecessary journeys to the main hospital, especially for the dressing of burns. However, it was essential to have close liaison between the central and peripheral hospitals.

Treatment in General Practice

Dr. D. L. CROMBIE (Birmingham) considered the treatment of accidents in general practice, and pointed out that the age and occupation of the patients had an influence on the pattern of their accidents. 4.8% of general-practitioner consultations were related to trauma, but probably a large number of the trivial injuries were treated by the lay public or medical auxiliaries. In cities patients tended to bypass their doctor and go direct to a casualty department; it had been found that 60% of all patients treated in such a department had sustained an accident, and of this group less than one-third required any service which could not be provided by a general practitioner. Further, sepsis developed less commonly in the wounds sutured in a general practitioner's surgery than in those treated at hospital. However, a general practitioner frequently found himself single-handed when emergencies occurred, and was further limited by the lack of *x* rays. A general practitioner was able to deal with injuries which did not endanger life in a cottage hospital, but Dr. Crombie made a plea that general practitioners should be kept more clearly informed of the facilities and latest advances in the main hospitals. Dr. C. T. MAITLAND (Ministry of Health) said the Ministry was concerned to see that all injured persons falling within the scope of the National Health Service should be treated with all the relevant medical knowledge available. There was often failure to utilize available medical knowledge for the benefit of society.

Despite the opportunity presented by the National Health Service for the organization and staffing of clinical services, major difficulties in staffing casualty and accident departments were reported. There was often, it seemed, lack of senior leadership. Many senior clinicians responsible on paper did not in fact undertake effective personal responsibility; among junior staff too much was often left to low-grade stepping-stone men; departments were often undermanned at all levels. What were the reasons for these discontents and inefficiency, he asked? Was it that the practice of accident surgery gave no training that counted for advancement, no assured future in a recognized specialty?

He felt that in many parts of the country there was need for a survey of the staffing and facilities. The staffing of these departments should be reviewed in relation to the responsibilities carried often in a supposedly 24-hour service. Then plans for functional area services could be prepared along the lines that had been described by the preceding speakers.

In the ensuing discussion Dr. W. N. LEAK (Winsford, Cheshire) made a plea that local general practitioners should be informed of the plans made to deal with major accidents in their areas. Dr. R. M. MCGREGOR (Hawick) suggested that general practitioners would welcome more guidance and

visits from the staff of their main regional hospital. Mr. B. O. SCOTT (Oxford) pointed out that £172m. was lost in 1956 as the result of the morbidity of road accidents alone, quite apart from the lost working-time. He also mentioned the difficulty in finding house-surgeons for accident work, and Dr. A. STAVELEY GOUGH (N.W. Metropolitan Regional Board) pointed out that a 24-hour service implied full consultant cover during these 24 hours.

Mr. J. S. BATCHELOR (London) and Mr. W. C. GISSANE (Birmingham) further emphasized that no accident case should be admitted to any hospital which did not have such consultant cover. Mr. H. J. SEDDON (London) briefly described the excellent organization of the medical services in Uganda, and compared the difficulties encountered when attempting to build up surgical services in the two countries. Mr. J. N. WILSON (London) suggested that it would be helpful to make a plan for dealing with accidents in the London area.

In summing up, Sir HARRY PLATT (Manchester) considered that in most areas adequate facilities existed for dealing with accidents, but that the underlying organization was in need of review. Accident centres and peripheral accident hospitals should be designated, with general practitioners trained in accident work.

SECTION OF OBSTETRICS AND GYNAECOLOGY

Wednesday, July 16

Dyspareunia

Professor H. C. MCLAREN (Birmingham), president of the Section, took the chair at a discussion on the problem of dyspareunia. The opening speaker, Professor A. M. CLAYE (Leeds), emphasized that dyspareunia was a symptom not of an individual but of a partnership. The husband must therefore be interviewed as well as the wife, but they should be seen separately. He felt strongly that the essential in prophylaxis was sane sex education of the adolescent, and that engaged couples should be encouraged to seek a premarital consultation. The ideal consultant was the general practitioner, and therefore the medical student should be taught how to tackle this work as well as how to deal with marital problems. The doctor must be neither shy nor hearty, and in dealing with dyspareunia must reassure both parties that the difficulty would be overcome. External dyspareunia was nearly always due to vaginismus consequent on fear, conscious or subconscious. Vaginal dilators succeeded only by virtue of suggestion, which could be carried out as successfully without their use. But sometimes it helped to have a physiotherapist instruct the woman in relaxation of the pelvic muscles. Internal dyspareunia was usually secondary and organic, due to the presence of a tender structure in the pouch of Douglas. Often, however, it was psychogenic, with frustration, boredom, and fear of pregnancy the commonest basic factors to be countered.

Physical Causes

Professor ALEC AGNEW (Vancouver, Canada) discussed the physical causes of dyspareunia. An organic condition might be the sole cause or contribute to a psychological reaction. Congenital lesions were a thick, undilatable hymen, vaginal septa (transverse or sagittal), and hypoplasia of the introitus. Fortunately all were amenable to surgical correction. Acquired lesions were more difficult to cure. The commonest antecedent was a gynaecological operation, particularly a repair. The surgeon, when operating, had therefore to bear in mind the preservation of the coital function. Acquired retroversion of the uterus causing dyspareunia, which it rarely did, could be corrected by a suspension operation. Endometriosis, especially if affecting the uterosacral ligaments or the pouch of Douglas, could cause severe dyspareunia, but the severity was not always proportionate to the palpable degree of involvement, although extension into the rectovaginal septum always led to intense pain. The treatment of endometriosis called for considerable judgment to determine whether hormonal therapy or conservative or radical surgery should be employed. Chronic pelvic infection with palpable masses also demanded surgical treatment. But in some cases the only positive findings were tenderness in the parametrial areas and pain on moving the cervix or uterus. Even in nulliparae these might be due to chronic cervicitis with spread of a low-grade infection into the surrounding tissues. For treatment, cauterization, conization, or amputation of the cervix was required.

Emotional Factors

Dr. SYLVIA MASSEY DAWKINS (London) said that, while physical lesions could produce emotional reactions, in many cases the pain or difficulty was psychogenic. The emotional factors varied at different phases in the life of woman. In the bride, previous physical or emotional trauma, feelings of guilt, taboos and fears of penetration, pregnancy and childbirth, and of male domination were known as possible underlying causes. In the wife and mother vaginismus secondary to slight physical lesions might be used as an excuse to avoid intercourse, while resentment against the husband or fear of further pregnancy might be the dominant factor in other cases. Preoccupation with the children and fulfilment in motherhood might also be relevant. In the postmenopausal years slight physical disturbances might produce disproportionate emotional reaction, while some felt shame at continued sexual desire at that time of life. Dr. Dawkins said that procrastination in seeking medical help was common. Both partners must be seen, so that there could be a full and frank discussion. Instruction in coital technique might be necessary or contraceptive advice indicated, but in some cases there was a need for psychiatric treatment.

There ensued a lively discussion from the floor. Mr. E. COPE (Birmingham) commented on the occurrence of postcoital colic as a symptom of an intrauterine lesion such as a polyp. He recommended the use of methylpentynol carbamate where anxiety added to coital problems. Mr. OSWALD LLOYD (Cambridge) advised the trial of a pessary if deep dyspareunia was associated with a retroversion. He thought that fear of pregnancy was the commonest aetiological factor in parous women. Professor W. C. W. NIXON (London) agreed, and further suggested special teaching clinics in medical schools and dyspareunia clinics in the hospitals to deal with the whole problem. However, two general practitioners, Dr. D. F. HEATH (Birmingham) and Dr. H. G. DOWLER (Gloucestershire) preferred to see their own patients about such intimate matters ; they would appreciate instruction and assistance rather than refer the patients to another hospital clinic. Professor CLAYE thought there was room for both, because, while some patients might prefer to discuss matters with their family doctor, others found it less embarrassing to see some doctor they did not know. Professor H. C. MCLAREN (Birmingham) discussed the difficulty of teaching students, some of whom were not mature enough to advise patients on such matters. Finally, Mr. W. G. MILLS (Birmingham) and Professor AGNEW agreed that it was important before performing hysterectomy to reassure the patient, and her husband, about the effect of the operation on their subsequent marital life.

SECTION OF ACCIDENT SURGERY

Friday, July 18

Prevention of Road Traffic Accidents

Suggestions for reducing the number of deaths and injuries resulting from road accidents were made by a well-contrasted group of authorities at a round-table conference arranged by the Section of Accident Surgery. The chair was taken by Mr. WILLIAM GISSANE (Birmingham), and the members of the panel were: Dr. R. J. SMEED (Road

Research Board), Mr. W. T. WILLIAMS (secretary of the Association of Motor Manufacturers and Traders), Mr. E. J. DODD (Chief Constable of Birmingham), Mr. G. F. ROWBOTHAM (Newcastle upon Tyne), and Mr. KEN RAWLINGS (a racing driver).

The first question drew attention to the losses sustained by insurance companies on car insurance. In the view of Mr. C. F. TRUSTRAM, chairman of the British Insurance Society, a further rise in premiums was only a matter of time if the present accident rate continued. Since 1926, 200,000 people—the population of a large town—had been killed on the roads, while some 5,500,000 had been maimed —two-thirds of Greater London's population. Mr. Trustram, interviewed by a national newspaper, had gone on to say, "Instead of thinking of the 'poor old motorist' when insurance rates go up, we should think of the 'poor old victim,' demanding safer roads." Mr. Trustram roundly blamed motorists for most of the accidents: "Inconsiderate, inexperienced, careless, and over-confident motorists are the sinners," and to prevent accidents and the cost of them to insurance companies he advocated the fearless imposition of penalties, including the banning of bad drivers.

"What can we do to deal with this particular problem?" asked the CHAIRMAN.

Mr. ROWBOTHAM said that the insurance companies did not realize how easily they were getting off with the expense of road accidents, because it was the Health Service that was carrying the monetary load. The Service would be able to build hospitals if it did not have to carry the medical costs of the insurance companies. His own clinic dealt with over 1,000 head injuries a year, each patient staying for three weeks, the cost of each bed being £27 a week.

More Discouragement Needed

Mr. DODD said that the insurance companies could do a great deal more in the field of accidents and in that of crime to make neither of them worth while. When preventive measures were advocated to deal with crime people were apt to say, "Why bother? Our property is insured." Rather the same attitude obtained with regard to accidents. Insurance rates went up every year because some people had far too many accidents. Those who had the accidents ought to be made to pay for them.

Dr. SMEED said the real trouble was that everybody thought somebody else ought to do something about it. The cost to the Health Service was not so very great. Medical and allied expenses were about £6m. a year, but the insurance companies drew in premiums to the extent of about £110m., so it would not make a very great difference if all the additional cost of the medical services was put on to the insurance companies. There was a lot to be said for that, but it was not the whole answer.

The CHAIRMAN said that in Birmingham the cost of efficient treatment was approximately 5% of the cost of the accident. Accidents cost the hospitals about £10m. a year, but they cost insurance companies about £150m.

The CHAIRMAN, dealing with queries from the floor about the cost to the Health Service of road accidents, said that payments to hospitals under the Road Traffic Act were so small that he had wondered whether it was really economic to employ a large number of secretaries to fill in so many forms to get a refund of some amount like 12s. 6d., which certainly did not cover the medical costs of a road accident.

Protective Devices

The next question, submitted by Dr. M. S. ROBERTS, was: "What further protection devices can usefully be fitted to motor-vehicles?"

Mr. WILLIAMS said that every manufacturer would wish to feel that the car he turned out was the safest car to drive. The Society of Motor Manufacturers was engaged in drawing up a code of practice for safety features in car design, points from which included: (1) that the external shape of the vehicle and fittings, including mascots and decorative trimmings, should be free from all sharp edges and projections; (2) that door-handles should be as nearly as possible flush with the body panelling and should not have obstructions which would catch in clothing; (3) that doors should be hinged at the front where practicable; (4) that the leading edge of the visors or cowls of headlamps should be designed to avoid sharp edges. Manufacturers were always seeking improvements, and, to a very large extent, were achieving them.

Asked by the Chairman for his views on protective helmets for drivers of sports cars and vehicles of high-performance and safety belts for passengers, Mr. ROWBOTHAM said there was no question but that the head helmet of Sir Hugh Cairns would save the lives of a large number of motor-cyclists. However, a lot of the helmets were becoming decorative. Their object was to bring the head slowly to rest, thus saving it from enormous physical distortion in the event of an accident. If made of decent material it would protect the skin and eliminate many of the dangers of infection. The real cause of accidents was the driver and his attitude; it was nothing to do with the vehicles on the road or the motor-car. People got injured because there was a driver using an internal combustion engine as a lethal weapon. If a car hit an irresistible object head on the person in the back seat would be thrown over the driver and his head would hit against the windscreen. It was the throw that killed passengers and not the crush, because on English roads it was very rare for vehicles to travel fast enough to cause a crush. In American road accidents the car was concertinaed, the doors opened, and the passengers were thrown out. He thought that all the evidence was in favour of having safety belts for passengers.

Mr. RAWLINGS said that the use of crash helmets was made compulsory by the rules of all racing competitions, but straps were not normally used; however, he would like to see them in motor-cars just as in aircraft.

Standard of Tests

To the question, "Should the standard of test for a road licence not be raised considerably?" Dr. SMEED agreed that it should be; the trouble was that nobody knew what qualities to look for which would prevent accidents. People did the wrong thing for temperamental and other reasons rather than because they did not know that what they were doing was wrong.

The CHAIRMAN said that research in American and Scandinavian countries on the suitability of transport drivers for industry in particular had shown that by reasonable tests the accident rate could be brought down, in some American companies by as much as 50%.

Dr. SMEED: "You can do a great deal if you have not got to worry about the justice of what you do. If you are prepared to say you believe that a driver is not going to be safe and therefore you will not employ him, you can go quite a way, but I don't think we can do that in general for car drivers. The public will not let you get away with it."

Mr. ROWBOTHAM said that that was the weakness of democracy. The Americans had selected their drivers not only physically but emotionally, and extended the bribe: "No accidents, higher wages"—something to their advantage.

Dealing with the next question: "Are present visual tests of a high enough standard? Does 'lazy eye' contribute to head-on crashes?" the CHAIRMAN said that the Canadians —who had worked the problem out very fully—believed that a lot of head-on crashes were due to faults in vision and faults in illumination linked up with vision; they had a good deal of evidence to prove that this was an important factor explaining those severe head-on crashes that occurred at dusk under certain lighting conditions, rather than epilepsy or alcoholism.

Mr. DODD warned against over-theorizing in such matters. Most of the accidents, in his experience, were due to "bad driving" and not to squints or anything of that kind.

Blood Alcohol Tests

The next question sought the views of the panel on whether blood-alcohol tests, as carried out in Sweden, would help to diminish road accidents. Mr. DODD said he was sure they would. However, it was a tricky business; the only person who could carry out the test was a doctor; it was not something that should be added to the duties of the police. But he doubted whether the British public would accept the methods adopted in Sweden, whereby if a certain percentage of alcohol was detected in the blood the driver concerned was sent to prison. Such a method, if taken really seriously, would undoubtedly reduce the number of road accidents. He was convinced that far more road accidents were attributable to alcohol than ever appeared in the statistics produced by any department.

Mr. ROWBOTHAM said that one of the difficulties was that there was nothing more difficult to prove than the obvious. The decision of whether or not a man was drunk should go to an impartial "jury," and if it was found that he was in fact unfit to be in charge of a car by reason of having taken drink then he should be dealt with severely. Mr. DODD said that far too many such cases were judged entirely on medical evidence, ignoring what had led to the person being examined by a medical practitioner. The sole object of medical advice should be to determine whether a person's condition was due to illness or some cause other than intoxication. The court should then decide the matter on the evidence of the police and independent witnesses who had actually seen what had happened and what had led to the person being arrested. A speaker from the floor said the doctor ought to be brought to the scene of the accident and not to the police station. A doctor should not be expected to tell whether a man was drunk or sober half an hour or an hour after the accident, when he might have sobered up somewhat.

Mr. ROWBOTHAM said that medical tests were undertaken solely for establishing whether there was disfunction of the cerebellum. There were few men of experience who did not firmly believe that they were able to detect even minor changes of behaviour or expression in their friends which resulted from imbibing alcohol. The eventual decision should be taken by an independent panel, partly on lay evidence and partly on medical evidence, not by the police or by a police doctor.

Mr. DODD said that, ideally, he would not disagree with that, but pointed to the difficulty of getting such an independent body of people together at 3 o'clock in the morning. It was difficult enough to get a doctor sometimes.

Professor A. P. THOMSON (Birmingham) said that the function of a doctor in such cases was to tell the court whether there was anything wrong with the man. It was quite impossible, when examining a man who was drunk, to say whether or not he had a physical disability. The proper time to examine him was the following day, when evanescent effects produced by drink or drugs would have disappeared.

Publicity about Accidents

The next question was: "Should there not be more publicity from the B.B.C. about accidents that have actually happened and the result of those accidents in terms of injuries?" Mr. RAWLINGS said that the sight of a wrecked car by the roadside was a most effective deterrent to over-speedy driving. Mr. ROWBOTHAM thought it was wise to let people know what was happening. There really could not be too much publicity about accidents. He thought that information should be given mainly in factual rather than dramatized form. Mr. DODD said the sad thing was that road accidents were no longer "news" and nobody cared about them. Mr. ROWBOTHAM said that was why the problem was essentially medical. Only the medical profession could attempt to explain that attitude. To make such an attempt would be the greatest piece of research that doctors could do, for he believed that it was the basic reason for the rise in the accident rate, and it involved a basic part of research that nobody had yet attempted.

The last question, from Mr. KNOX, of Birmingham, was: "What proportion of the published researches of the Road Research Laboratory are now concerned with road safety and how much is spent on road safety research?" Dr. SMEED said the total amount spent on road safety research by the Road Safety Council was probably of the order of £70,000 a year; but a certain amount of road safety research was done elsewhere.

Summing up the discussion, the CHAIRMAN said it was quite clear that the problem was one of prevention which those in medicine must tackle more seriously than had been done in the past. Considering the amount of money which accidents cost the country, £70,000 a year seemed an appallingly small sum to spend on road safety research.

Management of Severe Burns

The round-table discussion was followed by the presentation of two papers by doctors working at the Birmingham Accident Hospital. Introducing the speakers, the CHAIRMAN said that the hospital had been founded 17 years ago, attention first being directed, from a research and clinical angle, to minor injuries occurring in industry. During more recent years the research and clinical efforts had been concentrated on serious and multiple injuries.

Mr. DOUGLAS MACG. JACKSON (Birmingham) then presented his paper on "The Management of Severe Burns." The first thing to remember, he said, was that a severe burn was not just a severe type of surface lesion. The natural history of the illness initiated by a severe burn included oligaemia, renal ischaemia, and fluid and electrolyte imbalance. Bacterial colonization of the extensive wound might lead to septicaemia or graft failure with increasing weakness from pain and chronic malnutrition. Scarring could cause contractions to joints and subsequent deformities. The emphasis of modern treatment was directed towards preventing the natural sequelae and towards closure of the wounds as soon as possible.

The last decade had seen a steady improvement in techniques to measure the blood volume and electrolytes. As a result of more accurate diagnosis and better management of the shock stage, severely burned patients had survived longer, even if the mortality has not been greatly changed. The most lethal complication of severe burns in Britain was now infection, and attempts had recently been directed towards getting the better of it with earlier wound closure by surgery as well as with new and effective antibiotics.

Mr. Jackson then discussed the problems of diagnosis at successive stages of the management of severe burns: this included the diagnosis of latent shock, the colloid requirement of the patient, and the degree of red-cell destruction. Having outlined the evidence indicating that renal damage had occurred and that renal insufficiency was likely, he turned to the diagnosis of the depth of burning. The appearance was a very deceptive factor, even more so by the fourth or fifth day, at a time when most people would excise the burn. The pinprick method could be used to determine whether there were epithelial elements in the surface of the skin still alive. If the patient could feel a pin-prick in a burn it would heal within three weeks. Mr. Jackson concluded by making some suggestions on the prevention of infection.

Severe and Multiple Injuries

Mr. A. RUSCOE CLARKE (Birmingham) read a paper on severe and multiple injuries. With the increase of road accidents the pattern of civilian injuries was changing, so that those responsible for treatment were faced with a growing number and complexity of multiple and severe injuries. At the same time people were living longer, and even moderate injuries were an important cause of death in old people. A 10-year study of deaths at the accident hospital showed that in those under 55 about half the deaths in hospital from injury were associated with major head

injuries. The majority of the remainder had major damage to the trunk, often involving abdominal and thoracic organs.

Recent advances in the treatment of injuries included: (1) appreciation of the role of transfusion, and (2) an understanding of the need to maintain normal lung physiology. Death from injury confined to the limbs should be preventable except in the elderly, but transfusion and early surgery might be essential. Resuscitation of the more serious multiple and trunk injuries required transfusion, a knowledge of techniques of clinical and radiological diagnosis at the acute stage of injury, full facilities, and an expert team. Resuscitation of major chest injuries required detailed attention to the mechanics of lung function. This might involve bronchial suction, rib traction, or open surgery to fix the chest wall, tracheotomy, pleural drainage, assisted respiration, analgesia, or prolonged supervised narcosis. Even when the circulation and lung physiology were stabilized, major abdominal, and other surgery might be needed. A proportion of major injuries required very early surgery for internal bleeding. Massive transfusion might be essential, and its organization required special planning.

In many head injuries, particularly if other injuries were present, it was by no means certain that death was due solely to brain damage. Cerebral symptoms and even the effects of the brain damage were influenced by bleeding, the circulatory response to bleeding and injury, and anoxia and CO_2 build-up resulting from inefficient respiratory exchange. Head injuries, especially when associated with multiple injuries, required transfusion, a clear airway, bronchial suction, and often early tracheotomy in addition to detailed surgical and medical care of the head injury itself.

These advances in the treatment of major injuries required special facilities and the availability of an expert team immediately such patients reached hospital. It was inevitable that full facilities would be found only in major centres. In less specialized departments and in small outlying hospitals there must be some planning of the major first aid that could be given during the interval before the patient was sent to a hospital which had all the necessary surgical facilities, or a surgical team came to him.

SECTION OF ANAESTHETICS

Thursday, July 17

Dental Anaesthesia

With Dr. L. T. CLARKE (Birmingham), a vice-president, in the chair, Dr. R. E. LEE (Birmingham) gave a refreshingly vigorous review of the use of nitrous oxide for chairside dentistry. He described the method as a mixture of controlled asphyxia, some analgesia, and a great deal of hypnotic suggestion. Its main virtue was quick recovery, but he felt that, although nitrous oxide was the weakest anaesthetic gas in general use, it was not necessarily the safest. The fact that mortality rates were low was a tribute to the anaesthetist rather than to the method. There was probably much though unrecognized morbidity due to bad operating conditions or cerebral anoxia. How serious brief periods of cerebral anoxia might be Dr. Lee was not prepared to state, but he recalled the progressive mental deterioration which might occur in epileptics from repeated attacks of anoxia during their fits. To avoid these risks he suggested greater use of supplemental drugs, an adequate supply of oxygen, analgesia, a more careful psychological approach to the patient, and restriction of the extent of dental operations carried out in the chair.

Dr. D. S. YOUNG (Leeds) then discussed the place of intravenous agents in dentistry. They might be used in four ways: full general anaesthesia, with muscle relaxants, and a naso-tracheal tube might be chosen for major surgery and conservative work, which could then take place under ideal conditions; the use of an intravenous agent might be followed by nasopharyngeal intubation and nitrous oxide, but without relaxants; they could be the sole anaesthetic agent; or they could be used for the induction before continuing with nitrous oxide and oxygen, with or without supplemental agents. An intravenous agent had an immediate advantage over nitrous oxide in allowing a more pleasant induction, greater control of the patient and therefore better operating conditions, and the avoidance of anoxia. However, if these methods were to be used, the practitioner administering the anaesthetic needed even greater training than was required for nitrous oxide anaesthesia, and the consequences of a prolonged recovery must be fully explained to the dental surgeon and to the patient. Dr. Young recommended the addition of atropine to both thiopentone and buthalitone, since this would reduce secretions and also the incidence of laryngeal spasm. Intravenous anaesthesia was particularly suitable for multiple extractions, resistant subjects, the suspected difficult operation, and when the patient particularly requested it. However, a careful selection of patients was essential, and asthmatics and bronchitic subjects should be anaesthetized under hospital conditions. Recently it had been found that supplementing nitrous oxide with halothane reduced the amount of intravenous agent needed and allowed the concentration of oxygen to be increased.

Professor R. F. WOOLMER (London) opened the discussion by stressing the difficulties in training dental and medical practitioners in the art of dental anaesthesia. The whole question needed reviewing. Professor W. W. MUSHIN (Cardiff) suggested that the addition of atropine did not prevent laryngeal spasm *per se*, but only as a secondary effect following the reduction of secretions. He thought the training of doctors in anaesthesia should be done at the postgraduate and not the undergraduate stage. Dr. R. H. MOORE (New Southgate), Dr. W. N. ROLLASON (Hull), and Dr. L. T. CLARKE (Birmingham) also took part in the discussion.

Anaesthesia in the Tropics

Dr. VICTOR KEATING (Jamaica) described some of the anaesthetic problems he had encountered in the West Indies. They were not confined to British colonial territories, but had all been reported also from other parts of the world. With coloured patients the commonest difficulties were from failure to recognize cyanosis, a low haemoglobin due to malnutrition, unstable blood pressure, symptomless diabetes, and syphilitic arterial disease. A further problem in tropical countries was the change in temperature when a patient returned to a warm ward from an air-conditioned operating theatre. This often led to vasodilatation and a fall in blood pressure with all the appearances of oligaemic shock. The coloured patient seemed to have a different autonomic pattern from that of the white patient. Dr. Keating then showed slides illustrating some of the work done in Jamaica. These suggested that in the Jamaican general anaesthesia was followed by a considerable rise in blood sugar; and, further, that his adrenal cortex was much smaller than the accepted average, which might account for the relatively high mortality rate in these subjects. To offset these unfavourable factors the incidence of post-operative pulmonary complications was low. Dr. J. A. CARMAN (Nairobi) supported many of Dr. Keating's remarks.

Anaesthesia for Radiology

Under the chairmanship of Professor R. F. WOOLMER (London), Dr. J. R. E. JENKINS (London) presented a paper on anaesthesia for *x*-ray diagnosis. During an *x*-ray investigation for which an anaesthetic is required the radiologist demanded a quiet patient and the physician one whose physiological state is as near normal as possible. To achieve this, the anaesthetist must take into account the risk of explosion, excessive irradiation of himself, the condition of the patient, the effect of injecting contrast media into the patient, and the difficulty of assessing the patient's condition during darkness. The anaesthetist must be prepared for any eventuality, and he must be responsible for the condition

of the patient throughout the investigation. Dr. Jenkins illustrated with slides the difficulties encountered and the types of investigations required.

Cortisone and Anaesthetist

Dr. J. P. PAYNE presented a paper on cortisone and the anaesthetist. The physiology and pharmacology of cortisone and related compounds were reviewed. The high-molecular polypeptide corticotrophin was secreted by the pituitary gland and stimulated the adrenal cortex. Of the adrenal hormones, Dr. Payne said that, while the significance of the mineralocorticoids such as aldosterone might be uncertain, the glucocorticoids undoubtedly influenced most functions of the body. Naturally occurring hydrocortisone was 20% more active than synthetic, and its output was directly related to the plasma level of corticotrophin. To the anaesthetist the importance of these agents lay in the suppression and atrophy of the adrenal cortex which followed their continued administration. The greatest hazard occurred in emergency surgery as a rapid and apparently inexplicable deterioration of the patient's condition which did not respond to intravenous fluids with vasopressor drugs. Treatment with intravenous hydrocortisone and intramuscular cortisone should be started immediately and continued during the post-operative period.

A similar type of collapse had been seen in patients with healthy adrenal glands, which responded to cortisone therapy. Elective surgery in patients with known or expected adrenal insufficiency demanded supplementary cortisone treatment during and after surgery. Dr. Payne recommended that all patients should be questioned about previous cortisone therapy, and this should be entered on their notes.

SECTION OF CHILD HEALTH

Thursday, July 17

Vomiting in Infancy

With the president, Professor J. M. SMELLIE (Birmingham), in the chair, Dr. B. WOOD (Birmingham) opened a discussion on vomiting in infancy by analysing 100 consecutive cases in which vomiting without diarrhoea was the presenting symptom. Pyloric stenosis and other organic causes accounted for most, but left a group of initially uncertain origin. In just over half of them the cause became evident. Underfeeding he thought to be the major single cause, but mothers should be told that vomiting would not stop overnight with such treatment; these babies took time. Other causes were mismanagement and aerophagy. Although many paediatricians asserted that a breast-fed baby could not be overfed, he included two cases of "overfeeding" in his table, but explained that these infants were really gulping and were able to take an adequate amount of expressed breast milk perfectly well. The unexplained cases fell into two groups, "pseudo-pyloric" and "pseudo-oesophageal," and indeed some of the latter might have been examples of mild hiatus hernia. He thought that in all such doubtful cases treatment should be on the same lines as for hiatus hernia. Finally he referred to rare but treatable diseases such as the adrenogenital syndrome, galactosaemia, hyperchloraemic renal acidosis, and hypercalcaemia. In subsequent discussion Dr. BERYL D. CORNER (Bristol) drew attention to emotional tension between mother and baby as a cause of vomiting and of pyloric spasm which could be seen radiologically and which relaxed when the child was fed by a calm and experienced nurse. Dr. M. E. DISNEY (Birmingham) thought that the change from breast to cow's milk might cause vomiting until the baby became accustomed to the new food. Allergy might also play a part.

Tracheo-oesophageal Fistula

Mr. A. L. D'ABREU (Birmingham) discussed tracheo-oesophageal fistula. He said he was speaking somewhat irrelevantly, as in this condition babies never vomited. They regurgitated fine frothy mucus, coughed, and became cyanosed, especially during efforts to feed them. The last 40 cases of his colleague Mr. Keith Roberts (Birmingham) all showed these features. In 14 there was a firm maternal history of hydramnios, which might warn the obstetrician or midwife to consider the diagnosis. Even in cases where there had been much delay, treatment might be successful, for failure was not due to undernutrition but to pulmonary complications. These must be treated in the pre-operative period so that the lungs were dry at operation. The anaesthetist (the right anaesthetist: it was worth while to delay the operation if he or she was not immediately available) then intubated the trachea and applied suction before starting inhalational anaesthesia. In 37 cases treated by Mr. Roberts 28 had primary anastomoses, with ten deaths; nine had a first-stage operation, with four deaths; of the five survivors, three died after the reconstruction.

After discussion about the frequency of the condition, the PRESIDENT summarized the position: for every four cases of pyloric stenosis there was one of tracheo-oesophageal fistula. There were 100 pylorics a year at the Birmingham Children's Hospital, so there should be 20 to 25 fistulae, but in fact there were 10 to 14. Probably only half the cases were being diagnosed at present, but the number was rising.

Dr. T. MANN (Brighton) thought there were regional differences in incidence; in about 20,000 babies born in Brighton he had found only 4 to 5 cases in spite of careful search. Dr. MARY CROSSE (Birmingham) deplored Mr. d'Abreu's implication that diagnosis was not made before the baby had been given a feed. He agreed that such was not the case in units alive to the existence of the condition.

Intestinal Obstruction

Dr. A. GOUREVITCH (Birmingham) discussed intestinal obstruction in the newborn. Here vomiting of bile was the cardinal sign. He was appalled at the alarmingly high death rate in these cases, and with disarming modesty he led the audience in an exploration of the situation in Birmingham during the past ten years. Many factors were responsible for therapeutic failure, but the crux of the matter lay in the details of surgical technique. He felt that too many surgeons were operating on these cases—the neonatal belly was no more the place for the occasional surgeon than was the congenital heart. Mr. Gourevitch himself had concentrated on duodenal obstruction, with excellent results in cases of extrinsic obstruction and some improvement in cases of intrinsic obstruction. Miss ISABELLA FORSHALL (Liverpool) recommended duodeno-duodenal anastomosis in these cases, and (to the envy of other surgeons in the audience) reported complete success in cases of uncomplicated jejunal, ileal, and colonic obstruction.

Incompetent Cardia

Miss Forshall then introduced the difficult and debatable subject of the incompetent cardia. In 125 of her 130 cases vomiting started in the first two months (35 in the first week) of life, but the type of emesis was extremely variable. In about half her cases the lax cardia was below the diaphragm, in the others there was hiatus hernia. In eight there was also pyloric stenosis. In 25% of the others there was visible gastric peristalsis, and often vomiting was projectile. Presumably there was pyloric spasm, and she had found atropine methonitrate helpful. Surgical treatment was used in the worse cases of oesophageal damage, with improvement in half. Miss Forshall asked the audience for help (which she did not get) in avoiding stricture by medical or surgical treatment. She also wanted to know how one should follow these cases up and for how long. Would oesophagoscopy and examination of stools for occult blood remove the need for repeated *x*-ray examinations?

Dr. R. ASTLEY (Birmingham) described the use of radiology in the diagnosis of the conditions which had been discussed. He thought that lax cardia was always associated

with hiatus hernia, and illustrated his observations with cine-radiographs, which were received with rounds of applause. In the discussion afterwards the PRESIDENT asked whether hiatus hernia in infancy was related to the similar condition in adults. Various contradictory opinions were expressed, but Dr. ASTLEY described investigations in which by radiological study he had been able to find these hernias in two and even three generations.

SECTIONS OF CHILD HEALTH AND GENERAL PRACTICE

Friday, July 18

Psychological Disorders in Childhood

With the president of the Section of General Practice, Dr. H. W. DONOVAN (Birmingham), in the chair, Dr. LINDSEY W. BATTEN (London) opened an interesting discussion of psychological disorders in childhood. He said that Psyche had a finger in every pie and a fist in some, but it was a mistake to make a list of diseases and call them psychosomatic—several factors contributed to each illness. Allergy and psychosomatosis often acted together, but their highest common factor was the constitution of the patient. Dr. Batten entertained his audience with several striking examples wittily related. A facial eruption might be due to cosmetics, chrome salts, or conscience; the diagnosis could be deduced only from the history, signs, and course of the disorder, never from the static picture. Having made the diagnosis the physician must ponder it in his heart, for it was easy to do harm by mistimed explanation. The doctor should be a medical friend and adviser who won the confidence of parent and child, recognizing at least, and removing when possible, causes of emotional tension; instilling faith, courage, and expectation of a happy issue; and treating soma no less than psyche *secundum artem*.

Dr. S. ABRAHAMS (London) said that all illness had emotional overtones—the doctor needed a psychosomatic approach rather than a list of psychosomatic diseases. In childhood the somatic picture differed from that seen in adult life, and disappearance of the outward manifestations did not necessarily indicate that the psychological problems had been solved as the patient grew older. He related the history of a child with facial tics which recurred until the boy was 12 years old, when for the first time he felt he was a real person in his own right, no longer the shadow of his dominant father. Growing up involved stress, especially if the parents had high standards; the child had at times to kick away his supports beneath him, and then somatic symptoms might appear. The family doctor, by his understanding and handling of these problems, could play a limited part in their cure.

Dr. L. DULAKE (Reigate) thought that in many cases the damage was already done: all that the doctor could do was to mitigate its severity. Dr. J. WHITBY (London) said that they had to treat what was present at the time, without any preconceived ideas, for in the same patient different factors might act to produce similar clinical features at different times.

Problems in Adolescence

After some further discussion of the opening papers of the general practitioners, Professor J. M. SMELLIE (Birmingham) took the chair and introduced the first of the paediatric speakers, Dr. PARRY WILLIAMS (Coventry). Dr. Williams considered adolescent problems, for at this period of growth there were rapid changes in personality and physique. In attempting to become an individual in his own right the adolescent resented authority, but his resentment also made him feel unsure. The wide variations of normal growth and development were often not realized by parents; the doctor had to explain that puberty was reached two years earlier by girls than by boys, that obesity did not mean glandular deficiency, and so on. The sensitive adolescent needed sympathy and understanding in an unsentimental atmosphere.

Dr. J. P. M. TIZARD (London) discussed two approaches to child psychology. The psychoanalyst studied the whole psyche of few children, and his followers then applied these findings as general rules. The psychologist studied many children superficially; his general conclusions were then applied to particular cases. Dr. Tizard showed how either process might lead to misunderstanding, but in fact both methods were needed. It was wrong to conclude because one 2-year-old was miserable in hospital that all young children were miserable in hospital. By contrast a study of many children might lead to a conclusion that, in general, children's behaviour did not deteriorate after hospital admission, which could lead one to overlook the fact that a particular child had deteriorated seriously. Dr. Tizard embroidered these ideas with a wealth of example, epigram, and quotation before turning to a cogent examination of the part played by heredity in determining children's behaviour. Probably environment was more important, but neglect of inheritance had gone too far. As Dr. Batten had said in the discussion, men used to believe they were governed by a beneficent providence, now they had swung away from that belief and were faced with the alternative of belief in fate. This they could not bear, so they had substituted environment.

Child Guidance

After the paediatricians, way was made for the psychiatrist. Dr. R. F. BARBOUR (Bristol) reminded his audience that parents and child needed to be considered together in the child guidance clinic. In one situation the child might be stable and the mother intensely neurotic; in another the child might be neurotic and the mother calm and sensible. Adults decided when they felt ill; children had to convince a grown-up, and this weighted the scales in favour of the aggressive and naughty child, who was more likely to be treated than the introspective day-dreamer, who might be just as sick. Dr. Barbour detailed the main groups of disorders seen at a child guidance clinic, and remarked that doctors were often nowadays consulted about naughtiness in children and might wonder whether naughtiness was covered by the National Health Service Act. It might be relevant to remember that in a school for maladjusted children E.E.G. dysrhythmias were ten times as common as in children at other schools. If mental health was to be within the province of the general practitioner, he would have to concern himself with behaviour disorders: he used Snellen's types, so why should he be unwilling to use a vocabulary test, a reading table, and the Goodenough "draw a man" test? He could thus pick out children with educational difficulties, and if he also got the child to draw pictures of his own choice he would learn something of what went on under the surface of the child's mind—interpretation of the drawings would of course have to be learnt just as reading *x*-ray pictures had to be learnt.

SECTION OF DERMATOLOGY

Friday, July 18

Infantile Eczema

The session opened with the president, Dr. BERNARD C. TATE (Birmingham), in the chair for a round-table conference on infantile eczema. Members of the panel were Dr. R. T. BRAIN (London), Dr. P. D. C. KINMONT (Derby), Dr. J. K. H. MCCULLOUGH (Birmingham), and Dr. J. T. INGRAM (Leeds). Discussion ranged over terminology, incidence, the role of allergy, especially in relation to feeding, the influence of inheritance and of environmental factors, including the psychological. It was generally agreed that seborrhoeic dermatitis was a separate entity, though it might occasionally trigger off eczema. It was also felt that some degree of reasonable restraint was often necessary to

prevent damage by scratching, but a tar paste and the administration of sedatives were the main therapeutic requirements. Steroid hormones as yet were of limited value internally or locally.

There was subsequently a demonstration of interesting cases followed by a brief discussion.

Treatment of Warts

In an occasional paper on virus warts on the hands, Dr. R. B. COLES (Northampton) said that warts were notorious for their response to different and unrelated treatments, but spontaneous resolution might account for some of these cases. Patients with large numbers of warts recovered more slowly than those with few warts. Of 274 patients with warts on the hands, 230 were treated with Whitfield's wart lotion or salicyl collodion; 79 did not respond, and these, with the remainder of the series, required more radical measures. Of 248 patients seen six months after "clinical cure" 41 were not clear. Ultimately 14 remained uncured and 6 relapsed. Out of 29 patients who received no treatment the warts resolved spontaneously in 26. It was desirable to proceed with conservative treatment before contemplating radical measures. Dr. Coles had organized a team of about 100 "wart watchers" with a view towards a better understanding of the natural history and of the true value of treatment. It was probably necessary to review 10,000 cases to arrive at any valid conclusions.

Speaking on hypnosis in the treatment of warts, Dr. J. H. HARTLAND (West Bromwich) said warts often disappeared spontaneously and were susceptible to suggestion. In the hypnotic state the capacity to receive and act upon suggestion was increased. The deeper the hypnosis, the less critical the patient and the more quickly treatment succeeded. Treatment was given weekly or more frequently. Full explanation of the nature of hypnotic treatment was always advisable. Common multiple warts usually appearing on the hands and limbs responded well to this technique.

Diagnosis and Treatment of Fungous Infections

In a paper on diagnosis of ringworm of the extremities Dr. J. G. HOLMES (Coventry) indicated that interest in ringworm of the extremities in this country dated from 1911 when Whitfield put forward certain criteria for diagnosis and Malcolm Morris suggested that peeling and maceration between the toes was often due to ringworm infection. As a result of a field survey, conducted for the Medical Research Council with Mr. J. C. Gentles (Glasgow), the following conclusions were reached.

The clinical diagnosis of ringworm was difficult and required confirmation in the laboratory. Ringworm of the feet was commoner in those using communal baths. Maceration and peeling between the toes was sometimes due to constitutional eczema with or without bacterial infection and was rarely mycotic in origin, but some men had interdigital peeling and maceration without inflammation but with fungus present. It was probable that the parasite was living a saprophytic existence. Men with evidence of inflammation, such as redness or vesiculation, were mostly infected. The inflammation was due to a combined mycotic and bacterial infection. Ringworm of the hands was rare. In *Trichophyton rubrum* infection involvement of the nails was common and troublesome.

Dr. A. J. E. BARLOW (Huddersfield) said that accuracy of diagnosis should form the basis of all treatment of ringworm of the extremities. This was not always possible with fungous infections of the skin owing to lack of laboratory facilities, and it therefore became important that treatment should not be harmful to the patient. Owing to lack of knowledge of the factors controlling the parasitism of the ringworm group of fungi, the basis of present-day treatment rested upon the topical application of fungicides. In the thick horny layers of the palm and sole, problems of penetration arose; these accounted for the limitations of this method of treatment, because it was impossible regularly to obtain an effective concentration of fungicide at the site of active fungal growth. Laboratory assessment of fungicidal activity was of little use clinically, and the old-fashioned combination of salicylic acid with benzoic acid remained superior to the wide range of newer fungicides. This treatment was less costly and had the advantage of rarely causing irritation. Treatment of individual patients depended upon the clinical picture, and it should be realized that this was essentially the reaction of the host. The more acute the reaction the more the host was attempting to effect his own cure; hence there was less need for potent fungicides than when the host's reaction was minimal. Nail infection called for cultural identification and detailed investigation of the extent of the infection before surgical removal was contemplated.

A further paper on studies on the pathogenicity of the trichophyton species was read by Dr. C. N. D. CRUIKSHANK (Birmingham). With Dr. M. D. Trotter and Dr. S. R. Wood at the M.R.C. Unit for Research on the Experimental Pathology of the Skin he had been interested in the manner by which fungi of the trichophyton group produced clinical lesions. These fungi were non-invasive—that is, they multiplied in the keratin and epidermal part of the skin—and so the elaboration of diffusible substances must be of considerable importance in the pathology of the condition. Studies carried out on the biological effects of filtrates of cultures grown *in vitro* had shown the presence of a diffusible enzyme with proteolytic properties. This enzyme was active at body *p*H and capable of separating the epidermis from dermis and loosening the fine bonds between the cells of the prickle-cell layer. It was probably responsible for the itching associated with many clinical infections. Work had been carried out further to define the nature and behaviour of this enzyme. In addition there was a substance (probably a polypeptide) present in culture filtrates which was toxic to the tissues. Hypersensitivity was recognized as playing an important part in some fungal infections; studies to define accurately the substance responsible for the trichophytin reaction had been put in hand as a first stage towards the preparation of a trichophytin which could be accurately standardized and be free from the anomalous reactions usually associated with this test. Guinea-pigs had been sensitized by the injection of dried fungal mycelium and Freund's adjuvant, and fractions extracted from fungal cultures had been tested for allergenic activity.

Urticaria

In an occasional paper on the incidence of urticaria Dr. G. A. GRANT PETERKIN (Edinburgh) reported that in a period of five years 566 patients were diagnosed as having some form of urticaria: 300 had urticaria, 248 urticaria papulosa, and 8 urticaria pigmentosa. Only 24 patients below the age of 10 had true urticaria, and in the urticaria papulosa group only seven children were aged 10 years or more. Urticaria papulosa was most prevalent in the late summer months, though there was a high incidence in April and May. Ordinary urticaria itself occurred most frequently in May. In over 25% of patients with urticaria, drug sensitivity was the cause. More than half were due to penicillin, and the reactions often persisted long after the drug had been stopped. Aspirin was the cause in 20 of the 300 patients. A clear history of the asthma–eczema syndrome was obtained in only 5.66%, but in 18.6% the urticaria was attributed mainly to psychosomatic causes. In many patients antihistamine drugs had failed adequately to relieve the symptoms. It was surprising to find how effective autohaemotherapy had been.

Dr. R. P. WARIN (Bristol) discussed the treatment of chronic urticaria from the allergic and nervous aspects. Food and drug allergy often caused acute but rarely chronic urticaria. Of 10 cases in which chronic urticaria followed an acute attack, 3 were due to foods, 2 to serum injections, and 5 to penicillin. It seemed likely that the acute attacks triggered off a phase of chronic urticaria. In patients with chronic urticaria, aspirin and sodium salicylate made the weals and subcutaneous swellings worse, and this

effect appeared to be quantitative. Speaking of antihistamine drugs, he said that topically their only effect was anaesthetic. The action internally of equivalent doses of the different antihistaminics on urticaria was the same, though they had different side-effects. Drowsiness from antihistaminics was noticed more by intellectual workers. A not uncommon side-effect was restless aching of the limbs and sudden twitching of the legs at night. Fits had been produced in the potential epileptic, and convulsions occurred with poisoning by antihistamine drugs. The effect of antihistaminics on giant subcutaneous swelling was less than on dermal weals. When antihistaminics were discontinued weals returned unless the underlying tendency had passed. The continued suppression or reduction of the weals by antihistaminics did not appear to affect the tendency to urticaria. Cortisone and A.C.T.H. were reported as helping some patients, but in a carefully controlled series of 20 patients the effect was no different from that of inert tablets.

Dr. G. HOLTI (Birmingham) reported an investigation of 210 cases of urticaria, including measurements of the vascular responses and identification of specific sensitivity. During the active stage of urticaria dilatation of the skin vessels could be induced more rapidly and was more intense and more prolonged than in normal subjects, whereas vasoconstriction was impaired. Out of 210 patients tested, 125 suffered from other clinical conditions such as asthma, "hay-fever," and eczema, and their skin tests were not considered. In the remaining 85 patients positive skin tests to allergens were obtained in 54 (63%). This incidence compared unfavourably with results obtained in other allergic conditions like asthma, "hay-fever," and eczema, which may in part be explained by the fact that the prick tests used were often negative while intradermal tests gave clear-cut responses. Special investigation of 20 patients with chronic urticaria showed that all suffered from allergy, including 12 who were hypersensitive to yeasts. These patients responded strikingly to elimination diets; some of the yeast-sensitive patients required in addition the temporary administration of an oral fungicide. Most of these patients had chronic intestinal symptoms as well as persistent urticaria, and in a significant number the onset of symptoms was apparently related to the ingestion of antibiotics and sulphonamides.

SECTION OF GASTRO-ENTEROLOGY

Thursday, July 17

Chronic Diarrhoea

With the president, Dr. F. AVERY JONES (London), in the chair, a round-table conference was held on the subject of chronic diarrhoea. The members of the panel were Mr. B. N. BROOKE (Birmingham), Dr. C. F. HAWKINS (Birmingham), and Dr. W. T. COOKE (Birmingham).

The CHAIRMAN commented that classification of chronic diarrhoea was in many respects still unsatisfactory. In the early diagnosis of carcinoma of the colon the importance of full investigation was stressed; this should include barium enema, sigmoidoscopy, and repeated examination of the stools for occult blood. Should the diarrhoea continue it might be necessary to reinvestigate the patient after a period of two to four weeks, and laparotomy might be eventually justified for diagnostic purposes. Barium enemas sometimes failed to reveal an early carcinoma at the rectosigmoid junction or in the caecum, and the examination might have to be repeated.

In the diagnosis of ulcerative colitis proctoscopy was particularly useful, and in the obscure case rectal biopsy might be decisive. The disease could be mimicked by both steatorrhoea and regional enteritis. The frequency of the stools was a significant point: when the rectum was involved the patient would pass from 12 to 20 small stools in the day, whereas the number might only be 4 or 5 if there was no left-sided involvement. An example was the condition known as ileocolitis, in which only about six stools in the day might be passed, and on *x*-ray examination of the colon the maximum involvement was seen to be on the right side. In this condition steatorrhoea might be present owing to disturbed function of the small intestine, and liver involvement occasionally occurred. The absorption of vitamin B_{12}, however, was not affected. It was thought that ileocolitis might be an entirely separate disorder, distinct from both chronic idiopathic colitis and Crohn's disease.

The panel were agreed on the value of steroid therapy in ulcerative colitis and had found A.C.T.H. most useful. But long-term therapy with these drugs was not advised; they had to be given with care and could be dangerous by giving rise to deep lacunar ulceration, mucosal disintegration, dilatation of the colon, and perforation. There was an increased tendency after the use of these drugs for post-operative collapse to occur. Surgical treatment was indicated for the acute case which was deteriorating despite medical treatment, and after an acute complication such as perforation or a massive haemorrhage. It should also be considered in the chronic case in which there was serious disability, possibly complicated by the presence of anal fissures, polyarthritis, and skin lesions. The increased tendency to development of carcinoma of the colon was mentioned.

Steatorrhoea

A classification of steatorrhoea recommended by Dr. W. T. COOKE (Birmingham) was: (1) coeliac disease occurring in children and adults; (2) organic disease of the small intestine, including chronic inflammation and infiltration with neoplastic tissue; (3) post-gastrectomy diarrhoea; and (4) pancreatic insufficiency, which was not a common cause. Mesenteric lymphadenopathy did not give rise to steatorrhoea, for the development of which involvement of the intestinal wall was essential. In the diagnosis of steatorrhoea it was important to inspect the stools, which were usually bulky and buoyant, but could be of normal appearance. The blood should be examined and the small intestine *x*-rayed. If the stools contained more than 6 g. of fat in the 24 hours on an average diet, steatorrhoea should be suspected, and often it was not essential to carry out a strict fat-balance test.

The treatment of Crohn's disease should be primarily medical, in view of its tendency to self-limitation. A high-protein, low-fat diet, parenteral iron and vitamin B_{12}, and the use of steroids were all recommended. It was important to choose carefully the best time for surgical treatment, which should not be premature.

Chronic diarrhoea due to emotional disorders was relatively common, and the panel were of the opinion that the term "lienteric" diarrhoea should be abandoned. It was not infrequent to find that chronic diarrhoea was self-inflicted and resulted from chronic overdosage with such aperients as phenolphthalein and magnesium sulphate. There resulted a chronic loss of potassium which might lead to muscle weakness, coma, and even death. Infrequent causes of diarrhoea which had been encountered by members of the panel were pyloric stenosis and infestations with trichomonas and monilia.

Friday, July 18

Cardiospasm

Under the chairmanship of Dr. F. AVERY JONES (London), president of the Section of Gastro-enterology, a series of short papers were presented. Mr. G. H. WOOLER (Leeds) described the complications of cardiospasm and their treatment as seen in a series of 187 cases. Five patients had developed inhalation pneumonia, which might precede the symptoms of cardiospasm, and four patients had osteo-arthropathy. In two cases there was an associated oesophageal carcinoma and he had seen one patient with a large oesophageal diverticulum. Most patients with cardiospasm were very "oesophagus conscious," but a few were unaware

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In a recent clinical article (J.A.M.A., 1957, 163, 1115) it was stated that in a series of 2,511 cases in which 28 agents were tested in the symptomatic treatment of migraine, ergotamine tartrate was proved to be the most useful drug—and 81% of the patients showed improvement when ergotamine tartrate and caffeine were compounded with belladonna alkaloids. Orgraine applies the same successful principles of treatment.

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that they had dysphagia. He recommended dilatation with a Negus bag in the first instance, and if this measure failed he performed a Heller's operation with repair of the oesophageal hiatus. In only five cases had reflux oesophagitis been encountered. During subsequent discussion it was stated that peripheral neuritis and syncope might also be rare complications of cardiospasm.

Dyspepsia with Negative X-ray Findings

Dr. J. WHITBY (London), a general practitioner, had followed up a group of cases of dyspepsia with radiologically negative findings for from one to ten years. Of 27 such cases 14 were regarded on clinical grounds as suffering from peptic ulcer, and within three years the diagnosis was subsequently proved in four: in the remaining 13 of the 27 cases nervous dyspepsia was diagnosed, and only one patient subsequently developed a proved peptic ulcer. He believed that potential ulcer subjects might either develop an ulcer or have a neurotic episode clinically indistinguishable from ulcer. In these radiologically negative cases the somatic symptoms might be followed and replaced after an interval by a frank anxiety state. It was of little value to carry out an *x*-ray examination to reassure neurotic subjects. Of 22 *x*-ray-negative subjects suspected of having gastric carcinoma, nine were subsequently found to be suffering from depression. Chronic gastric symptoms could be the presenting feature in cases of involutional melancholia, and might persist for as long as six months before the diagnosis became apparent. In contrast to his experience with stomach disorders, the speaker had encountered many patients with abnormal cholecystograms who were entirely free from dyspepsia.

Peptic Ulcer and Coronary Sclerosis

Dr. G. WATKINSON (Leeds) had studied the relation of chronic peptic ulcer to coronary sclerosis and to gall-bladder disease by means of two necropsy surveys. The first of these was of 13,000 examinations performed in Leeds between 1930 and 1949; in a second, national survey, the results of 7,000 examinations carried out in 1956 in nine towns in England and Scotland were analysed. To balance merits and defects in the series the findings were compared with the frequency of coronary disease occurring in populations without ulcer, in those with ulcers found by chance, and in those of ulcer deaths. In both surveys coronary disease was encountered significantly more commonly and more severely in men with chronic peptic ulcer and even more so in chronic duodenal ulcer. The similarity of the age distribution of the associations found in the two surveys, together with the high levels of significance observed, increased the likelihood that a true relationship existed. Coronary infarctions also occurred in one survey with a significantly increased frequency in young and middle-aged men with ulcer, and again particularly with duodenal ulcer. Excessive numbers of coronary disease and infarction occurred in men between the ages of 55 and 64 years with chronic gastric ulcer but could not be found in any other age group. The two surveys had also shown gall-bladder diseases to be significantly less common in both men and women dying from all types of chronic peptic ulcer.

Chronic Pancreatitis

The diagnosis and treatment of chronic relapsing pancreatitis, said Mr. R. SMITH (London), must be based on an accurate appreciation of the anatomy and physiology of the normal pancreato-biliary apparatus and the deviations from normal in disease. Reflux of infected bile into the main pancreatic duct was an important causative factor. In chronic pancreatitis, a cholangiogram would demonstrate reflux into the duct, the outline of which was distorted and dilated. Reflux was due to delay in the escape of bile into the duodenum. Each attack of pancreatitis predisposed to the next by causing damage to the duct epithelium which permitted the escape of ferments into the gland substance. He recommended sphincterotomy in the treatment of early cases, reserving the more hazardous procedure of pancreatoduodenectomy for the intractable case with severe incapacity. In reply to a questioner, the speaker remarked that pancreatic biopsy was sometimes useful in the differential diagnosis from pancreatic neoplasm: it was best performed through the medial wall of the duodenum.

Regional Ileitis

Dr. W. T. COOKE (Birmingham) defined regional ileitis as a benign non-tuberculous granulomatous lesion of unknown aetiology which was most frequent in the second and third decades and ran a long course fluctuated by acute exacerbations. About 20% of cases gave a history of symptoms extending over a few weeks only; in others, an ischio-rectal abscess or chronic ill-health with recurrent subacute obstruction was a frequent presenting feature. Seventy-five per cent. of patients relapsed within 10 years. Useful indices of progress were the patients' weight, the erythrocyte sedimentation rate, and the serum albumin level. Many patients had a low plasma ascorbic acid, a low serum iron, and a low or normal serum vitamin-B_{12} level. Folic acid deficiency did not occur unless the proximal small intestine was involved. Treatment should be medical throughout, but in nearly all cases surgical intervention was required at some time for the relief of obstruction or intractable anaemia, or to remove fistulae. By-pass intestinal operations should be avoided. Steroid therapy might be useful in some cases, but its precise indications had not yet been defined.

Iatrogenic Liver Disease

In a communication on iatrogenic liver disease, Dr. A. E. A. READ (London) found it a salutary experience to study lesions of the liver and biliary tract produced by the medical profession. Certain drugs, of which chlorpromazine was the best-known, might cause an intrahepatic obstructive jaundice which, if prolonged, might lead to the patient running the risk of abdominal exploration to exclude an intrahepatic bile-duct lesion. All previous medication should be carefully noted in jaundice patients. An incorrect diagnosis of liver disease in the harmless condition of congenital hyperbilirubinaemia might lead to the development of a neurosis. Recurrent cholangitis often resulted from operative strictures following cholecystectomy or common-bile-duct exploration. Portal cirrhosis should never be diagnosed by laparotomy, which was particularly dangerous in the presence of jaundice or ascites. Hepatic coma might ensue, and could also be induced by the ill-advised use of morphine in alimentary haemorrhage, by high protein diets, and by ammonium chloride, acetazolamide, and chlorothiazide. In chronic liver disease no drug could be used with complete safety; barbitone was preferred only because its action was potentially reversible. A personal series of cases of hepatic coma were described and iatrogenic factors were found to be important in 34% of them.

SECTION OF GERIATRICS

Friday, July 18

Falls in the Elderly

With the president, Dr. J. H. SHELDON (Wolverhampton), in the chair, Dr. C. A. BOUCHER (Reading) opened a discussion on falls in the elderly by quoting some national statistics. 73% of fatal home accidents occurred to people over 65 years of age, and 58% to those over 75. Women fell more often than men, and the greater number of falls happened at home. 63% of all fatal accidents at home were the result of falls, and the death rate from this cause was steadily increasing. Non-fatal falls in old people often caused serious incapacity, and loss of independence and of personal confidence. The large numbers were causing embarrassment to the hospitals. The highest death rate from falls

in old people was in Scotland, with progressively lower rates in Northern England, the Midlands, and the South. The reason for these differences was not known. The majority of falls took place when the victim was standing or moving on the level, not on the stairs. A number occurred in hospital during rehabilitation. Environmental factors such as loose rugs and polished floors were of great significance.

Dr. MACDONALD CRITCHLEY (London) contributed a paper *in absentia*, which was read by Dr. L. NAGLEY (Birmingham), on the causation of falls. In a small number of cases impairment of consciousness was responsible, whether of cardiac or "cerebral" origin. A larger number were due to transient imbalance, including acute vertigo; the elderly were especially sensitive to barbiturates. A third, though rarer, cause was the "drop seizures" of the elderly, which took place without warning or loss of consciousness. The explanation of these was in doubt, though some suggested impairment of basilar artery circulation; their control was difficult. The largest group comprised falls from defective powers of locomotion, which involved several sensory and motor functions. A further group suffered from simple loss of confidence, shuffling along with small steps while clutching at bystanders or furniture, yet improving with encouragement.

Mr. L. Z. COSIN (Oxford) discussed the problems of rehabilitating the elderly in the light of their tendency to fall. After even 14 days in bed wasting would be added to the muscular insufficiency of old age. Many hemiplegic patients suffered a disturbance of body-image, so that they incorrectly imagined they were walking properly upright. Similarly, those with hemianaesthesia and proprioceptive loss were at a disadvantage. Those with permanent flaccidity or incoordination after strokes needed callipers and instruction in slow, deliberate walking. Failure of muscular relaxation was important as a cause of imperfect gait and falls. Finally, a significant number developed a fear of falling which precluded rehabilitation and sometimes had a profound effect on the total personality.

The PRESIDENT and other speakers raised the question of inadequate lighting in private houses as a cause of falls. General discussion ranged over the causation of falls in hospital and the significance to these of polished floors and shortage of nursing staff. Falls out of bed were said to be common, and the merits and demerits of cot beds and low beds were considered. Dr. J. N. AGATE (Ipswich) believed that those who were apt to fall should be taught techniques of rising again, since many even when uninjured lay on the floor, perhaps a whole night. Dr. P. D. BEDFORD (Oxford) appealed for open-mindedness in considering the classification of "attacks" and falls, about the real cause of which there was so often much doubt.

SECTIONS OF GERIATRICS AND PSYCHIATRY

Friday, July 18

Confusional States in the Elderly

The two Sections met jointly under the chairmanship of Dr. J. H. SHELDON (Wolverhampton) to consider confusion and other mental abnormalities in the elderly. Professor MARTIN ROTH (Newcastle) defined a confusional state as one of delirium with variable clouding of consciousness, with delusions and hallucinations, and characteristically an affect of fearful apprehension. Physical illness coexisted in many cases of mental disorder in the elderly of whichever variety, and caused diagnostic difficulties, especially where the mental state did not respond when the physical disease was treated. Thus the mental diagnosis should be based principally on the nature and progression of the psychiatric symptoms. A sustained depressive mood usually meant a depressive psychosis. Physical illness was not only the trigger to mental disorder: it contributed materially to affective and senile psychosis. Those who survived into old age were tough personalities and fell ill only in the face of physical breakdown.

Dementia and delirium were not synonymous, and the latter was seldom the precursor of the former, though once dementia had shown itself confusional states often supervened. When delirium came out of a clear sky without neurological signs, the cause was an acute and potentially reversible disease. Furthermore, delirium was characterized by short duration and rapid fluctuations with agitation, hallucinosis, and positive incorrect beliefs, whereas dementia usually had the opposite characteristics. The state of delirium might indeed be evidence of a homoeostatic mechanism at work against brain damage, as was suggested by such evidence as the fluctuations, the high survival rate, and the E.E.G. patterns. In practical terms, confusional states should first be admitted to general hospitals. Practitioners should be careful to give the history of the physical illness too. Quietness and sympathetic skilled nursing were essential in treatment.

Dr. P. D. BEDFORD (Oxford) considered the problem more from the medical standpoint, and drew a sharp distinction between confusion and dementia, which latter should never be diagnosed without full evidence, because of the stigma and the implications of irreversibility. No sharp demarcation existed between normal mental age-change and dementia, and many mentally deranged old people could be kept happily in their own accustomed environment. We should have particular regard to the natural history of ageing of the mind, and recognize the reversibility of confusional states. Old people should not be taken into mental hospitals unless they were likely to respond to the treatment available there, or if they exhibited severe and persistent behaviour disorders. In fact 80% of admissions to the Oxford Geriatric Unit were mentally disturbed; yet the mortality of these did not differ from that in the mentally normal patients admitted. Dr. Bedford discussed the possible reasons for confusion being so common in the elderly, and for the fact of slow and incomplete recovery. It was vital to regard the confused patient as really ill.

Social Competence

Mr. L. Z. COSIN (Oxford) discussed the epidemiological aspects, and described some of the conclusions of the Nuffield mental health research team. Analysis of the histories of 50 permanently confused patients suggested that there was an appreciable load of intellectual deterioration being borne which did not get early enough to the notice of the family doctor. The longer the victims were left, the worse the outlook. Mr. Cosin introduced the concept of the "social competence" of elderly patients with mental disturbances, and showed how it could be restored by treatment but often relapsed when treatment was withdrawn.

Dr. RONALD G. GIBSON (Winchester) put a general practitioner's viewpoint. He was sure the State must learn to maintain the intellectual abilities of the individual and should not permit rigid retirement policies. He recognized certain particular types of people in particular social classes as most liable to confusional states in old age. The practitioner's duty was to create the right attitude of the family to the mental disorder. The value of a hospital stay, even if temporary, was in the occupational therapy, the gentle discipline, and the time the nurses could devote to listening to and encouraging the elderly.

Dr. W. F. ANDERSON (Glasgow) wondered how many cases of mental disorder in the elderly were kept hidden as the family skeleton in the cupboard. He had found former unskilled workers especially vulnerable, and advocated retirement preparation schemes. Dr. W. N. LEAK (Winsford, Cheshire) wondered how far radio, television, and clubs could provide prophylactic mental stimulation. Dr. R. V. DENT (Manchester) had found how important restoration of vision was, but how disappointing hearing-aids were, in fending off senile mental disorders.

SECTION OF NEUROLOGY AND NEUROSURGERY

Thursday, July 17

Neurological Disease in Pregnancy and the Puerperium

With the president, Professor BRODIE HUGHES (Birmingham), in the chair, Dr. J. PURDON MARTIN (London) opened a discussion on neurological disorders in pregnancy and the puerperium by reading a paper on "Puerperal Cerebral Venous Thrombosis." He said that the cerebral vascular lesions which occurred during pregnancy were mostly arterial and had particular associations. As examples he cited cerebral haemorrhage with arterial hypertension, subarachnoid haemorrhage with cerebral vascular malformation, and cerebral embolism with auricular fibrillation. However, the vascular lesions which occurred in the puerperium were nearly all venous.

The cause of intracranial venous thrombosis occurring in the puerperium or after abortion (and sometimes during pregnancy) remained a mystery. It usually declared itself suddenly a week or more after a normal delivery; it was seldom fatal, but deaths occasionally occurred. Veins in the surface of the brain were found swollen and filled with thrombus, and there might be clots in the superior longitudinal sinus. Underneath there was haemorrhagic infarction of the brain, of variable extent. Symptoms fell into three groups—namely, convulsive, paralytic, and those of intracranial hypertension. The first aim of treatment was to arrest convulsions, if present. If anticoagulants were used, it must be with the full knowledge that haemorrhage was already present beneath the obstructed veins. Dr. Purdon Martin referred also to the necrosis of the anterior lobe of the pituitary gland which might occur during pregnancy, or, more often, in association with post-partum haemorrhage.

Dr. HELEN DIMSDALE (London) discussed the problem presented by epilepsy in the pregnant woman. She said that improved treatment and social management had resulted in greater opportunities for the marriage of epileptic women, and hence epilepsy was likely to become an increasingly common complication of pregnancy. The effect of pregnancy was, however, unpredictable. Attacks might increase in number, change in character from minor to major, or be unaffected. A reduction in incidence was usually related to better therapy, as metabolic changes which normally occurred in pregnancy, such as hydration, increased ventilation, and dilution of calcium, sodium, and magnesium in the serum, favoured an increase in the number of fits. The occurrence of more frequent seizures might be preceded by an excessive weight gain or sodium retention. Dr. Dimsdale said that when attacks first appeared in pregnancy (gestational epilepsy) they were likely to be partial or focal in character. When patients developed fits as a manifestation of toxaemia of pregnancy a genetic or constitutional factor was usually present, and such patients might continue to have fits afterwards. She also stressed the occasional difficulty of distinguishing between status epilepticus (which might be the first manifestation of a cerebral dysrhythmia) and eclampsia. The treatment of epilepsy must take the form of suitable anticonvulsants with the dosage corrected for gain in weight. Excessive weight gain should be controlled by diet, and anaemia, if present, should be treated. In status epilepticus, continuous intravenous thiopentone might be required.

Disseminated Sclerosis in Pregnancy

Professor P. C. P. CLOAKE (Birmingham) read a paper on disseminated sclerosis in relation to pregnancy. He said that there was a widespread belief that onset or relapse in disseminated sclerosis was especially apt to be associated with pregnancy and the puerperium. This view had been questioned in recent years on the grounds that a comparison between the frequency of onset or relapse during this state and their frequency during the other years of the child-bearing period had revealed no significant difference in incidence. Professor Cloake said that in examining the case histories of 174 female patients with disseminated sclerosis he had found no evidence that onset or relapse occurred more often during the pregnancy-puerperal year than in other similar years of the child-bearing period when the patient was not pregnant. Hence, from the statistical point of view, his findings tended to support current opinion. On the other hand, from a careful examination of individual case histories he had come to the conclusion that pregnancy could not be considered to be entirely innocuous in its effects upon the disease, at least not in every case. He went on to consider in detail the advice which should be given to unmarried, married, and pregnant patients with disseminated sclerosis. While a great many factors must be taken into account in each individual case, and there were no rules which were universally applicable, it appeared that significant deterioration or relapse might be expected in a small proportion of cases during pregnancy, and more particularly in the puerperium

The next paper, by Mr. J. M. SMALL (Birmingham), was devoted to a consideration of the effects of pregnancy upon tumours and anomalies of the nervous system. Mr. Small pointed out that certain conditions of this type might be specifically affected by pregnancy, with subsequent recession. He recalled that during pregnancy there was fluid and salt retention, largely resulting from the secretion of oestrogen and progesterone by the placenta. The blood volume increased strikingly up to the seventh month of pregnancy, as did the platelet count and plasma fibrinogen, but the serum proteins and blood viscosity were reduced. Spider naevi commonly appeared during pregnancy but faded during parturiiion; these were probably due to the high level of circulating oestrogen, and a similar cause might account for their presence in neonates. Furthermore, the pituitary gland, and particularly its anterior lobe, might increase to about twice the normal size. It was probably physiological changes of this nature which accounted for the repeated attacks of neurological disability during pregnancy, each succeeded by remission of symptoms after parturition, which occurred in some patients with intracranial neoplasms and vascular anomalies. Certainly meningiomata, angiomata, and neurofibromata might behave in this manner. Parasellar meningiomas were particularly apt to do so. Similar exacerbations might occur in patients with spinal meningiomata and angiomata. Mr. Small described a number of illustrative cases and pointed out that the exacerbation of symptoms was always clearly related to peaks of oestrin and adrenal corticoid secretion and to fluid retention. He then considered briefly the problems which arose in the neurosurgical management of such cases.

In the final paper of the morning Mr. J. E. A. O'CONNELL (London) described the forms of lumbo-sacral palsy which might complicate pregnancy. He recalled that weakness in one or other lower limb following labour had been recognized for many years and had generally been attributed to sacral-plexus injury resulting from pressure from the foetal head or from obstetric forceps. However, he recalled that in 1944 he had described four cases in which weakness of a lower limb developed early in the puerperium and was shown in each case to be due to a lumbar disk protrusion. Of 1,100 patients with lumbar intervertebral disk protrusion operated upon in the past 20 years, 347 (31.5%) were women, and 90% of these were of child-bearing age. In the latter group 179 (51.5%) had had one or more pregnancies, and in 70 (39.1%) of them symptoms of the disk protrusion arose in association with pregnancy. Symptoms arose before delivery in 42, during labour in 8, and during the puerperium in 20. Clearly, therefore, the risk of intervertebral disk protrusion was increased during pregnancy. Mr. O'Connell went on to analyse in detail the degree and extent of muscular weakness which occurred as a result of disk prolapse in these cases, and showed that weakness was more likely to occur and to be more severe in pregnant than in non-pregnant women. Thus it was evident that the prolapsed intervertebral disk was an important cause of obstetric

lumbo-sacral palsies; however, from his highly selected material, Mr. O'Connell did not feel able to assess the relative incidence and importance of this and other causes.

SECTION OF ORTHOPAEDICS

Friday, July 18

Tuberculosis of the Spine

Mr. F. G. ALLAN (Birmingham), vice-president of the Section, was in the chair when Mr. M. C. WILKINSON (Braintree, Essex) opened a discussion on the treatment of tuberculosis of the spine. He recalled the rapid improvement seen in children suffering from spinal tuberculosis when moved out of the cities into long-stay orthopaedic hospitals a quarter of a century ago, and he compared those changes with those brought about by antibiotics and chemotherapy. It was now possible, and indeed often essential, to operate on tuberculous lesions of the spine when intervention would have been disastrous in former times. Mr. Wilkinson reminded his audience that Hippocrates had given a better prognosis for spinal disease below the diaphragm than above, and many series of cases had since shown the great need for improvement, particularly in the treatment of tuberculosis affecting particularly the thoraco-lumbar and the lower and mid-thoracic regions of the spine. In addition to constitutional therapy and chemotherapy, direct operative treatment was necessary to remove caseous material, disk and cartilage remnants, and sequestra, all of which prevented sound and rapid healing. After operation further bone destruction did not occur, and a return to normality could be expected. The operative mortality in over one hundred cases had been nil, and the only morbidity had been in two cases with transient pneumothorax. Recurrence of the disease after operation (usually performed on cases likely to respond unfavourably to conservative measures alone) was much less than in patients not subjected to operation.

Mr. R. ROAF (Oswestry) drew attention to the difficulties in assessing the effects of treatment because the disease was pleomorphic and variable. The virulence of the organisms and the patient's natural resistance had also to be considered, a tuberculous focus always indicating that the patient's resistance had broken down. In addition to measures to improve general health, rest, and chemotherapy, operations to remove necrotic tissue were required to give antibiotic or chemotherapeutic agents a chance to act in most favourable circumstances. A few years ago Mr. Roaf had limited surgical intervention to the drainage of abscesses, but he now advised operation as early as possible —though pathologically speaking this was at a late stage. At operation he aimed at being as radical as possible in the removal of necrotic debris. Afterwards the patients showed marked clinical improvement. Streptomycin was used locally at the time of operation, and given systemically for the following three months. P.A.S. and isoniazid were given for six months. Patients with lesions in the lumbar spine were usually kept recumbent for three to four months after operation; in the case of the thoracic spine this period was five to eight months.

Mr. D. E. MACRAE (Alton, Hants) confined his remarks to cases with new disease, and compared a group treated by surgery and antibiotics with a group treated in exactly similar circumstances but without operation. Disease affecting the cervical spine was the most rare, but also the most dangerous because of the instability of this part of the spine. A two-stage operation was advised, the spinous processes and laminae first being secured temporarily by wire, and then thorough curettage of the diseased tissue being undertaken by approaching it behind the carotid sheath. In the thoracic spine immediate operation was the treatment of choice; it reduced the likelihood of spread up and down the spine, decreased the period of hospitalization, and gave a better prognosis with less chance of recurrence. Mr. Macrae advised exploring the spine from both sides at the same operation, as he had encountered bilateral abscess cavities which had only poor intercommunication. In the lumbar spine the prognosis was good with conservative treatment alone, and operative intervention was confined either to cases not responding to general measures or to those with a localized focus of infection in bone. In addition to its therapeutic value, exploration of the spine was sometimes useful in confirming the diagnosis.

In the subsequent discussion Mr. F. G. ALLAN warned the meeting of the difficulties of these operations which had given such brilliant results. Mr. H. J. SEDDON (London) was in agreement with the three speakers, but inquired about distinguishing sound and unsound ankylosis. Mr. M. C. WILKINSON pointed out that these were rather arbitrary terms and that the distinction was clinical rather than radiological. Dr. H. J. T. ROSS (Birmingham) suggested that operation might not be necessary if adequate courses of chemotherapy were given, possibly extending over three years, but Mr. R. ROAF thought this would be impracticable. Both he and Mr. WILKINSON pointed out that bone lesions had sometimes been seen to progress while the patient was being treated successfully with chemotherapy for some other tuberculous lesion.

Artificial Limbs for Children

An occasional paper was read by Dr. D. S. MCKENZIE (Roehampton) on artificial limbs for children. He stressed that, although children with lower-limb amputations or congenital abnormalities would walk with almost any sort of equipment, surgery had to be planned in relation to the ultimate function with a prosthesis. In the case of the tibia, fibula, and humerus, the greater growth occurred at the proximal end and so produced a cone-shaped stump; in the case of the femur shortness of the bone was a problem. Dr. McKenzie advised that a child should be given an adult type of prosthesis rather than a peg-leg, which resulted in poor gait and had a bad psychological effect on the child, particularly when going to school. Only a small minority of these children were not able to attend normal schools. A leg prosthesis should be given soon after the child attempted to stand, and required renewal as growth occurred. Instruction in the use of an artificial leg was unnecessary until the child was much older and took pride in its appearance. In the case of an artificial arm instruction was essential as soon as the child was old enough to be taught and had been provided with a functional prosthesis. Sometimes it was not wise to enclose a child's arm in a prosthesis, thereby depriving it of tactile sensation, but if it were decided to supply one this should be done very early in life before the child had become "one-hand-minded." As in the case of lower-limb prostheses, artificial arms had to be renewed as growth occurred. Mr. R. ROAF (Oswestry) suggested that frequently children with congenital defects of their arms were more skilful using their stumps than prostheses.

Congenital Dislocation of Hip in Adults

Mr. P. A. RING (London) in a paper on the treatment of congenital dislocation of the hip in adults pointed out that the condition was uncommon—in fact, records of only 62 cases had been found in eight of the London teaching hospitals. He had excluded cases in which the dislocation had been reduced in childhood. Arthrodesis had been performed successfully with relief of pain and improvement of function in five of the six cases in which it had been carried out as a primary manœuvre; but following failed arthroplasty bony ankylosis was secured in only one of the four cases. Cup arthroplasty had been performed on 17 hips, of which two had good, pain-free movement. Ten more of these patients had little pain, but were virtually immobile. The femoral head had been excised and replaced by a prosthesis in six cases, of which only one was not a failure after six years. Many varieties of osteotomy had been performed, but on the whole the results were disappointing: though pain had often been eased the functional activity had not been increased.

Mr. Ring suggested that, for a unilateral case or a bilateral one with symptoms in one hip only, arthrodesis was the best treatment, and, though cup arthroplasty could give almost as good results, these were uncertain. For a case with bilateral symptoms there was no satisfactory treatment.

Mr. M. H. M. HARRISON (Birmingham) inquired whether any of the cases had been treated by excision of the head and neck without osteotomy, but there were none in this series. Mr. J. S. BATCHELOR (London) mentioned the difficulties of arthrodesis in these cases.

SECTION OF PATHOLOGY AND BACTERIOLOGY

Friday, July 18

Preparation and Use of Virus Vaccines

In the morning, with the president, Professor J. W. ORR (Birmingham), in the chair, there was a discussion on the preparation and use of virus vaccines. Professor C. H. STUART-HARRIS (Sheffield) described the preparation and use of inactivated virus vaccines. Virus vaccines were no different from bacterial vaccines in the way in which they worked. They depended for their effectiveness upon the production of antibodies in the inoculated person. Sometimes the antibody response was elicited by the use of an attenuated live virus. Inactivated virus vaccines were prepared from viruses in which the infective properties had been destroyed without impairing the antigenic properties. Cultivation of viruses for vaccines presented special difficulties because of the large amount of virus needed and because it must be relatively free from non-viral constituents, which could be eliminated by filtration or centrifugation. Some viruses—for example, influenza virus—had to be concentrated before use as an antigen. The fertile hen's egg was the best culture medium, but the number of human viruses which could be cultivated on it was very limited. The best strain of virus had to be chosen both for its antigenicity and its virulence. In this respect viruses could be divided into those in which there was only one antigenic species—for example, the smallpox vaccinia viruses—and those, such as the Coxsackie virus, which existed in great diversity. Viruses of which there were only a few strains, such as the poliomyelitis virus, presented no problem, since polyvalent vaccines could be prepared. It was more difficult to prepare vaccines of viruses like the influenza virus which, in addition to antigenic diversity, showed evolutionary change in their antigenic composition. The strain of virus responsible for the previous epidemic was nowadays usually incorporated, but this would not confer protection against the current infection as was found with polyvalent influenza vaccine in the recent epidemic of Asian influenza. As to virulence of the virus, fortunately there was no direct relationship between antigenicity and virulence.

There were many methods of inactivation of viruses. Formaldehyde inactivation was the most popular, since it distorted the structure of the virus less than any other methods. Our lack of knowledge of the mode of action of inactivators made mass preparation of vaccines, such as poliomyelitis vaccine, which was dangerous unless fully inactivated, more difficult. Standardization of the vaccines was also difficult, since not only did potency and antigenicity have to be standard but the vaccine had to comply with safety standards as well. The dosage of vaccine depended on the amount of virus antigen present in the vaccine, and this was difficult to determine.

Live Vaccines

Professor G. W. A. DICK (Belfast), discussing the safety and protection afforded by live-virus vaccines compared with inactive-virus vaccines, said that there were three prerequisites for safety of live vaccines: the development of attenuated strains, their testing in animals, and then their testing in humans. So far as yellow fever was concerned, only the 17D tissue culture and egg-adapted virus was safe and did not cause yellow fever in monkeys, though it was encephalitogenic on intracerebral inoculation. Vaccine lots of 17D virus were initiated from primary or secondary seed lots because of the tendency of the virus to mutate on repeated subculture to a strain encephalitogenic to humans. Probably virulent variants of the virus arose in the body after inoculation, but could do no harm because they were blocked by avirulent particles and because antibody developed so quickly.

There were two living rabies vaccines—that of Pasteur, and the egg-adapted Flury virus, which was apparently safe possibly because it did not multiply in human tissues. In the case of living poliomyelitis vaccines the aim was to produce strains of virus with minimal affinity for primate neurones. After development such strains were fed to adult volunteers, and, more importantly, to young children, in whose bowels the poliomyelitis viruses multiplied best. The amount and type of virus recovered in the excreta were studied in order to ascertain the risk of spread to and infection of the rest of the community. It was impossible to compare the safety of live with that of inactive virus vaccines in smallpox and yellow fever. With adequate safety tests killed poliomyelitis virus vaccines were relatively safe, but there were no comparable data for live vaccines.

There was little to support the view that live-virus vaccines conferred as durable an immunity as a natural infection. After infection with poliomyelitis the level of antibody in most people declined, and the same happened after administration of living attenuated oral vaccines. Indeed, antibody levels after giving living oral vaccines were lower than after vaccination with Salk vaccine and much less than could be attained by a third boost dose of Salk vaccine. It might not be desirable to decrease the transmission of poliomyelitis vaccines, since natural infections might be of great importance in maintaining herd immunity and were the first mechanism of defence against the paralytic disease.

Need for Rhesus Monkeys

Dr. T. H. FLEWETT (Birmingham) said that, while the supply of monkeys needed to make polio vaccine was adequate now, they were expensive and inconvenient. A stable cell line capable of supporting virus growth and being propagated indefinitely would be most useful. HeLa cells, however, being derived from a human cancer, were plainly unsuitable. Cell lines, all of which would support polio virus growth, had been derived from human liver, intestine, conjunctiva, amnion, and skin, and also from monkey and embryo-rabbit kidney. All except one of these (the MK 1 line established from a monkey kidney by Westwood and his colleagues at Porton) had a morphology very similar to that of HeLa cells, and the suspicion of *in vitro* malignant change therefore arose. The MK 1 line resembled fresh monkey kidney tissue cultures in appearance but differed from them in that its cells were subtetraploid; moreover, it showed a higher proportion of giant cells and abnormal mitoses than primary cultures. A proportion of tetraploid cells were found in normal tissues, however, and it appeared to be these that were best adapted to life *in vitro*. The usual cytological criteria of malignancy applied to cells fresh from the body might well not be applicable to tissue cultures. The only real test was how cultured cells behaved when inoculated back into the appropriate animal. So far, the MK 1 line looked the most promising, with the embryo-rabbit kidney line as runner-up. But much more work remained to be done before any of these could be accepted for general use. The rhesus monkey was not redundant yet.

Use and Abuse of the Hospital Laboratory by Hospital and General Practitioners

Dr. J. D. ALLAN GRAY (London) said that the enjoyment by general practitioners of the clinical pathology services worked for the good of clinical pathology. The laboratory services were useful to hospital practitioners but rather less so to general practitioners, though in certain fields, such as

haematology, they were invaluable. Meetings of local branches of the British Medical Association were vital in initiating and fostering the essential liaison between the general practitioner and the clinical pathologist. Publications by the *British Medical Journal* such as *Clinical Pathology in General Practice* indicated to the general practitioner just how much help he could expect from his local pathologist. The interest of the general practitioner in pathology could be stimulated by week-end clinico-pathological meetings. He did not think that the pathological services were particularly abused except by newly qualified house-officers and occasionally when pathological tests were duplicated on the same patient passing through the different departments of the hospital. In general, he concluded that judicious use of the services of the pathology and *x*-ray departments by general practitioners prevented flooding of out-patient sessions and hospital beds with patients who could more appropriately be treated at home by their own family doctor.

Dr. PATRICK KIDD (Worcester) emphasized that it had always been the policy of the British Medical Association to give the general practitioner access to pathological and *x*-ray services. In his own laboratory all specimens submitted by general practitioners were examined. He held a clinical pathology out-patient session to which general practitioners could send patients, and he always welcomed visits from his colleagues in general practice. 10% of all the specimens he examined came from general practitioners, and, of these, examinations of sputa comprised the largest number, though other common requests were for blood counts, Wassermann reactions, and pregnancy tests. He would like to see more examinations of nose and throat swabs. As an illustration of the value of the clinical pathology service to general practitioners he said that only 4 out of 500 cases of iron-deficiency anaemia known to him in his area had to come into hospital. All the same, he found many normal results on materials submitted by general practitioners and suggested that most large practices could afford a grey wedge haemoglobinometer, by the use of which some unnecessary blood counts could be avoided. He thought that the pathologist could be of more help to the practitioners than at present in the diagnosis of urinary and respiratory infections, and he entered a plea for more blood counts in late pregnancy. More could be done in the field of anticoagulant therapy by close consultation between the family doctor and the pathologist. For the future he hoped to see collaboration between the general practitioner and the clinical pathologist in research. There was little abuse of the laboratory, though sometimes general practitioners referred patients as a kind of placebo or to clear a surgery quickly on a heavy day. In hospital the blunderbuss investigation and the fashionable test were abuses of the laboratory service, and far too many leucocyte counts on children were requested. There was occasionally failure to consult the pathologist before embarking on elaborate investigations.

In the discussion which followed, Dr. W. WEINER (Birmingham) said that more use should be made of the blood transfusion laboratories. He did not think the pathological services were abused.

Neoplasia Induced by Radiation

During the afternoon a symposium was held on neoplasia induced by radiation. Professor D. H. COLLINS (Sheffield), a vice-president, took the chair, and Professor G. M. WILSON (Sheffield) gave the first paper on irradiation and cancer. He had investigated all the cases of thyroid carcinoma which had occurred in Sheffield between 1946 and 1956. Of these patients, 12 had developed thyroid carcinoma under the age of 35 years, 6 of whom had been exposed to radiation in infancy or childhood. The site of the cancer, which was normally a papillary carcinoma, was closely related to the area which had been irradiated. The radiation dose varied from 130 to 2,700 r, and the latent interval between irradiation and the appearance of the cancer was from 5 to 18 years. Out of 91 patients treated by *x*-irradiation for thyrotoxicosis between 1931 and 1945 none had so far developed carcinoma of the thyroid. But, of 160 patients of less than 20 years of age who had undergone irradiation of the neck for benign conditions, three developed thyroid carcinoma. There was a highly suggestive correlation between irradiation of the neck and subsequent development of thyroid carcinoma, though the evidence was clearer when irradiation had taken place in childhood than in adult life.

Dr. ALICE STEWART (Oxford) had followed up approximately 1,299 of the 1,600 children under the age of 10 dying of cancer between 1953 and 1955. Control interviews by their own family doctors were held with 1,300 children comparable so far as possible with those in the test group. Nearly half the deaths were due to acute leukaemia. There were no deaths from carcinoma of the thyroid in children of less than 10 years old. In no case had a mother received therapeutic *x* rays during the relevant pregnancy. Diagnostic radiographs were mostly of the abdominal region of the mother and mostly taken in the second half of pregnancy in the control series. In the fatal cases approximately the same number of mothers had undergone diagnostic radiography in the second half of pregnancy, but many more had had diagnostic radiography in the first half of pregnancy than in the control series. Besides the leukaemias, only the neuroblastomas and teratomas seemed to be particularly likely to develop after maternal irradiation. Comparatively few children were *x*-rayed after birth, but of those who died of leukaemia many more than in the control group had been *x*-rayed in infancy. The peak of mortality from leukaemia in childhood was at 4 years of age, and this had been getting worse during the last few years. There was some evidence that the effect of antenatal *x* rays could persist after the age of 10, whereas the *x* rays of infancy seemed to hasten the date of death.

Dr. A. W. G. GOOLDEN (London) said that, of a large number of mostly young patients treated by irradiation of the neck for benign conditions, 45 had since developed cancer of the pharynx, six cancer of the larynx, and one cancer of the thyroid. The latent interval between irradiation and development of pharyngeal cancer varied from 10 to 38 years, with a mean of 26 years. Patients who developed pharyngeal cancer showed all degrees of radiation damage to the skin, varying from practically none to severe. Thus there was evidence that carcinogenesis could be initiated even in tissues which had not suffered severe radiation injury. Most of the patients affected were women, and 60–70% of the tumours occurred in the hypopharynx, with an unusually high incidence in the group aged 40–50 years. He concluded that the adult thyroid was relatively insensitive to radiation compared with that of an infant, in which carcinoma could develop after comparatively small doses of radiation.

In the discussion Professor J. W. ORR (Birmingham) expressed surprise that radiation did not play a part in the genesis of the commoner types of cancer. Professor WILSON said that the reason that radiation tumours did not occur in the commoner sites was because the pre-conditions for their development—namely, treatment by irradiation for benign conditions, and a long latent interval between irradiation and the appearance of the tumour—did not hold in the more common sites of cancer development.

Neuropathy Associated with Carcinoma

Dr. W. T. SMITH (Birmingham), discussing neuropathy associated with carcinoma, said that neurological complications of secondary growth might be due to macroscopic metastases in nervous or adjacent tissues; to microscopic focal deposits or microscopic diffuse infiltrations with malignant cells, in which case the brain appeared normal macroscopically; or to metastases confined to the subarachnoid space, which might give rise to progressive dementia such as was seen most commonly in patients with primary carcinoma of the stomach.

Primary carcinoma could infiltrate neural tissue directly; it could induce nutritional neuropathy—for example,

Wernicke's encephalopathy secondary to carcinoma of the stomach or large intestine ; or it might infiltrate organs such as the liver.

Neuropathy could also be induced by emboli or malignant cells. These could be macroscopic or microscopic, the latter being a well-recognized complication of carcinoma of the bronchus.

Carcinomatous neuropathy due to an associated thrombotic syndrome was characterized by venous and occasionally arterial microthromboses sometimes affecting the heart valves. The cerebral vessels might be the first to be implicated. Clinically limb or cranial nerve palsies, fits, mental changes, aphasia, and ataxia occurred. Primary carcinoma of the pancreas was most commonly associated with this syndrome, in which characteristically the coagulability of the blood was unchanged and anticoagulant therapy was without effect.

Unexplained or classical carcinomatous neuropathy was of various clinical types, but most commonly sensory or cerebellar. Lesions of the sensory type were confined to the dorsal root ganglia and the spinal cord. In the cerebellar type the molecular layer of the cerebellum was thin, the Purkinje cells disappeared, and astrocytes proliferated. Unexplained neuropathies were usually associated with primary growths of the bronchus, except for the cerebellar disturbance, which was associated with primary growths elsewhere as well. Non-metastatic neurological complications of cancer were often the first clinical indication of the disease, and the recognition of their nature could lead to early diagnosis and treatment of the growth.

SECTION OF PSYCHIATRY

Thursday, July 17

Periodic Psychoses

With Dr. ELIOT SLATER (London), president of the Section, in the chair, Dr. J. L. CRAMMER (Birmingham) read a paper on periodic psychoses. He said that these were mental illnesses in which there was a regular series of attacks of schizophrenic or manic-depressive, or even hysterical or psychopathic, symptoms, comparable in rhythm with the periodic bleedings of the menstrual cycle, though found in both sexes. Such periodicity might begin at any age, sometimes after a year or so of non-rhythmic psychotic illness, and then remained very stable year after year, with occasional brief remissions. He thought there were one or two such cases tucked away in the back wards of every mental hospital and that they should be studied because the recurring pattern of illness with normal intervals facilitated detailed investigation. Such cases probably always showed physical abnormalities in association with their mental cycle, changes in bowel and bladder habit, pulse rate, and particularly in body weight. He described in detail two cases. The first was a man with a six-day cycle, two days inactive and semi-stuporous followed by four days of increasing overactivity, which had been repeating itself for five years or more. Inactivity was associated with oliguria and a gain in body weight, overactivity at first with a polyuria and loss of body weight. By dietary control and fluid balance measurement it seemed inescapable that there was a fluctuation in body water linked in some way with the changing mental state. A second case had had a six-weeks cycle for several years—about two weeks hypomanic followed by two weeks' depression and two weeks' normal interval. In the middle of the depressive phase there was a short phase of a mixed state when both hypomanic and depressive symptoms were present together, and this too was heralded by a loss of body water and body weight, with later recovery. In both patients, estimation of the 24-hour urinary excretion of 17-hydroxycorticoids by the Norymberski method showed adrenal cortical underactivity during hypomania, hyperactivity during depression.

These chemical and clinical abnormalities might be epiphenomena or actively involved in producing some of the mental symptoms. Later experiment, but particularly the study of more cases by more workers, would clarify this.

In the subsequent discussion Dr. E. S. STERN (Warwick) thought that psychotic attacks occurred quite randomly and that a psychological cause could always be discovered ; while Dr. M. HAMILTON (Leeds) questioned both these views, the first because it was susceptible of precise inquiry by calculation and was not a matter of opinion, and the second because it was not a hypothesis capable of test. Dr. M. SIM (Birmingham) and the PRESIDENT thought that periodic psychoses certainly occurred, while Dr. B. MANDELBROTE (Gloucester) was doubtful.

Methods in Drug Trials

Dr. A. D. HARRIS (Birmingham) then spoke on drug trials in chronic mental patients, describing aspects he and Dr. F. Letemendia (Birmingham) had specially considered in preparing a long-term chlorpromazine trial in a group of 28 hitherto untreated chronic psychotics. This trial was still running and would cover about 18 months. It was double-blind, with 14 patients receiving the drug and 14 a placebo, and the treatments had been exchanged at half-time. Before starting the trial proper they had carried out several months' intensive observation to make sure the patients were well stabilized in their chronic mental state, whatever it might be, and not changing under the influence of the special attention they were getting.

During this time an experiment on observer-suggestibility was carried out. The nursing staff had to report weekly on various aspects of the behaviour and appearance of each patient. After a time half the patients were given 100 mg. of nicotinic acid daily, enough to cause a transient facial flush. It took seven weeks for the nurses to notice that ten of the patients so treated were flushing, and thereafter they also recorded flushing in a few of those not receiving the drug. However, this had no influence on their other assessments.

In another inquiry each patient was shown his full-face photograph mixed up with those of other patients. (This had originally been intended as a device to get the patients to talk about one another.) A proportion of the chronic schizophrenics so examined recognized the pictures of others but failed to identify their own portrait, and this seeming difficulty with their own body image could not be related to severity or length of illness, while they had ample opportunity to see their faces every day in mirrors while shaving.

From the patients' assessments of one another very useful material was obtained. Nurses' assessments were of value only when they were questioned orally about specific aspects of the patients. Inquiry had shown that many of the patients still received regular visits from relatives, even after 20 years or more of hospitalization, and these visitors were another valuable source of information about the course of the patient's illness. However, the final burden of assessment lay on the medical workers, and periodic interviews with each patient had been recorded on tape for later comparison, in hopes of maintaining constancy in observer standards.

One other important point which had emerged was the difficulty of matching control and treatment groups satisfactorily. Initially they had been matched for age, severity of illness, and length of stay in hospital. Later, when weight and blood pressure became of interest during the trial as physical indices of change, their starting values were analysed and the two groups found to be significantly different at the 5% level for these measures. This illustrated how difficult it was to plan a controlled trial, except from previous experience in an uncontrolled one of the sort that the textbooks always condemned.

Dr. B. MANDELBROTE (Gloucester), Dr. J. R. MATHERS (Birmingham), Dr. M. SIM (Birmingham), and Dr. M. HAMILTON (Leeds) took part in the discussion.

General Practitioner's View

The meeting then heard Dr. ALFRED MODEL (Stockport) give a general practitioner's view of drug trials. He felt that these were impossible in general practice because of the difficulty of assessment at short occasional contacts with patients, even if many practitioners united in the trial, perhaps under the auspices of the College of General Practitioners, as was being done in a study on epilepsy. The individual practice had too few psychotics. He and his partner had 4,500 patients, of whom 9 had had one or more schizophrenic attacks, and more than half of these had been mental hospital in-patients. There was difficulty in getting agreement over diagnosis. While he agreed with Dr. C. A. H. Watts (Leicester) that depressions were the commonest complaint, he thought most of them were neurotic, not endogenous. In three months he reckoned 27% of surgery attendances in his practice were for psychiatric reasons in the widest sense, but this took account of the "by the way" syndrome, his name for patients who came ostensibly for a physical complaint, and who, just as they were leaving, threw out casually a reference to some mental trouble they had, which might be much more serious than the physical ill.

In treatment he used chlorpromazine a little, reserpine less and less; he preferred the older sedatives, even bromide mixtures, to the newer drugs offered on the market, because the old were quite as effective as the new. A placebo bottle of medicine was valuable because it was a way of keeping an eye on a patient, getting him to attend regularly for his bottle to be refilled. He remarked how encouraging it was to find general practitioners invited to take part at all meetings of the Section of Psychiatry.

SECTION OF SOCIAL AND PREVENTIVE MEDICINE

Thursday, July 17

Public Policy and Personal Health

The president, Professor THOMAS MCKEOWN (Birmingham), opened the meeting by explaining the purpose of the symposium. He pointed out that the great advances in preventive medicine during the last century had been made in respect of environmental influences such as water supply and housing—factors which were capable of control by legislation. There were, however, many important environmental influences the control or modification of which had to remain very largely a personal matter. It was the purpose of the meeting to consider some of these features of the personal environment and to inquire whether it was possible or desirable for public policy to contribute to their control.

Effects of Radiation

Professor BRIAN MACMAHON (New York) opened with a paper on "The Effects of Diagnostic Radiography in Adults." He said that the production of genetic change in plants and the lower animals by radiation, even in small doses, was well authenticated. It was not possible to measure this effect in man, but there was every reason to believe that it existed. For a number of reasons this must be regarded as highly undesirable. He believed that medical radiation accounted for an appreciable proportion of the deaths from leukaemia to-day. This was a relatively rare disease, however, and the absolute risk of leukaemia associated with diagnostic radiography was small. In his opinion the appropriate action in relation to these risks was to speed up researches on the subject, to standardize radiographic equipment, to decide on a public policy limiting routine chest radiography, and to make physicians more aware of the risks involved.

Dr. ALICE STEWART (Oxford) spoke on "The Effects of Diagnostic Radiography in Children." She summarized the results of her own and related inquiries into the harmful effects on the child of obstetrical *x*-ray examination. She pointed out that this involved the exposure of the whole body of the foetus to a relatively big dose. There could now be no doubt that a proportion of the children so exposed developed malignant disease and leukaemia. The risk involved appeared to be about one death before the 10th birthday for every thousand exposures. The earlier in pregnancy that *x*-ray examination took place the greater was the risk. Her recommendations were that the efficiency of *x*-ray plant should be controlled and improved, that doctors ordering obstetrical *x*-ray examination should always bear the risk in mind, and that the practice of using *x*-ray examination as a routine procedure in pregnancy should be discontinued.

Exercise and Health

Dr. H. M. SINCLAIR (Oxford) spoke on the subject of "Exercise and Health." He began by referring briefly to experimental studies on lower animals, children, and adults. In his view many of the chronic degenerative diseases in middle and late life were related to a relative dietary deficiency of essential fatty acids. Lack of exercise resulted in obesity, and in man the process of becoming fat appeared to be associated with high levels of serum cholesterol and phospholipids. If an excess of calories was ingested, body fat was laid down mainly in saturated fats. An excess of this type of fat greatly increased the requirement of the essential fatty acids, and so was likely to result in a relative deficiency.

Dr. Sinclair then referred to epidemiological studies on the relation of exercise to health. These clearly indicated that the more sedentary a man's occupation the more likely he was to develop coronary disease. Once again he related this to the obesity caused by inactivity. His conclusion was that lack of exercise was relatively unimportant as a cause of ill-health compared with the obesity that so often accompanied it, and that the solution was "girth control."

Alcohol and Road Accidents

Professor W. S. WALTON said that there was a growing concern in this and many other countries about the problem of alcohol and road accidents. In 1956 there were 216,172 road accidents brought to the notice of the public. Of these only about 5% were officially recorded as due to alcohol. But this low figure was due to the difficulty of obtaining a conviction within the framework of the present Road Traffic Act. It was generally well known that alcohol was responsible, in whole or in part, for many more accidents. He said that in his opinion the following measures were called for: more publicity by the press, the B.B.C., television companies, and voluntary societies with regard to the effect of even small doses of alcohol upon driving capacity; a review of road traffic legislation; the defining of more precise standards—for example, blood alcohol level—and better training of medical students in medical jurisprudence.

Food

Professor JOHN YUDKIN (London) concluded the symposium with a paper on "Food and the Individual." He said that the advice given by doctors to patients about diet was often no more based on sound nutritional knowledge than were the guesses of the layman. Doctors had not been taught to answer the sort of questions patients asked. This was particularly true about reducing diets and slimming products. As a result lay people turned to magazine articles and proprietary advertisements. These were often ill-informed or based on fallacies. Sometimes they were even harmful. He believed that public action was called for. In his opinion the *British Medical Journal* should not accept advertisements for proprietary slimming products, and the British Medical Association should set up a panel of experts to examine the credentials of such products and to give certificates to those meeting with approval.

ROUND-TABLE CONFERENCE

Wednesday, July 16

THE FATHER'S PLACE AT THE CONFINEMENT

Mr. OSWALD LLOYD (Cambridge), a vice-president of the Section of Obstetrics and Gynaecology, took the chair at the Round-table Conference on "The Father's Place at the Confinement" and introduced the members of the panel: Dr. BARBARA PARKER (Birmingham), Professor W. C. W. NIXON (London), Miss N. DEANE, a midwife (Bristol), and Mr. P. C. BARKLA (Nottingham).

In answer to the chairman's first question, the panel members were unanimous that the husband had no inalienable right to be present at his wife's confinement. Miss Deane emphasized that the wife's wishes in the matter should be paramount, and Mrs. Parker pointed out that some wives felt strongly that the husband should not be present. Professor Nixon agreed in principle, but added that ideally a hospital should be without bars, and that husbands should be welcomed, with certain reservations. At home the husband was often invaluable in assisting the midwife, but in his hospital the husband was allowed to attend the confinement only if the couple had attended a preliminary class of explanation and were both agreed on the desirability of the husband's attendance at the labour.

Miss Deane had found at her hospital that after the preliminary discussion of the point some husbands had acquired such confidence in the hospital staff that they no longer asked to be present at the confinement. Mrs. Parker had found that the wife was often unduly concerned at the presence of her husband; while he might be a help and comfort in the early hours of labour, there was no place for him in the late first and in the second stages. However, she would like to make it possible for every father to see his wife and newborn baby as soon after delivery as possible. Mr. Barkla emphasized that most women preferred to appear at their best before their husbands. They took pride in tackling their own peculiar task of maternity on their own. He himself did not believe that many women wished their husbands to be present throughout labour.

From the floor, Mr. W. G. MILLS (Birmingham) considered the position when the husband was a doctor. They all knew how difficult it was to decide when to exclude him if minor complications arose. The chairman thought that the personality of the individual husband must be taken into consideration, but Professor Nixon was opposed to any husband being present at an abnormal labour. It was generally agreed that the husband was often useful as an extra pair of hands during the first stage, especially if there was a shortage of midwives. But Professor H. C. MCLAREN (Birmingham) was forthright in his comments on this point: the husband might be of some help, but he was also a considerable responsibility. On occasion he was even a nuisance, requiring to be watched, gowned, nourished, and to some extent protected.

The conference ended with a vote being taken. This showed that only a small minority would exclude the father from the confinement, but it was apparent that many more would not allow him to be present during the second stage.

THE SCIENTIFIC EXHIBITION

[FROM A SPECIAL CORRESPONDENT]

Once again the Scientific Exhibition proved a great attraction for members and visitors at the Annual Meeting. As an exercise in postgraduate education it has a value all its own, for, unlike the set sessions, it allows the individual doctor to assimilate knowledge at his own speed.

A great debt is owed to all responsible for the individual displays, which covered a wide range of subjects, and to Mr. B. N. BROOKE, the honorary secretary of the exhibition. The appreciation of the members was shown by their close interest in the exhibits and by the large following which attended the President on his official tour of the exhibition on Wednesday afternoon, July 16.

Good as the exhibition at Birmingham was, however, there is still scope for improvement in the future in two respects: first, stalls dealing with the same or similar subjects should be grouped together; and, secondly, and this is more important, if more floor space could be provided those inspecting one exhibit would not have to stand right against the display in the opposite booth and so interfere with the view of others.

Neurology

Pride of place this year was taken by neurology, exhibits on the medical and surgical aspects of which constituted almost a quarter of the total exhibition. The department of neurosurgery, United Birmingham Hospitals, illustrated the theory and technique for bilateral temporal lobotomy for psychomotor epilepsy. The Midland Centre for Neurosurgery and the Queen Elizabeth Hospital of Birmingham demonstrated the anatomy, technique, post-operative care, results, and rationale of hypophysectomy in the treatment of cancer of the breast. Those interested went on to see the operation on the colour television programme of Tuesday, July 15. The appropriate departments of the United Birmingham Hospitals depicted the electroencephalographic changes in respiratory diseases and discussed their significance, as well as illustrating the condition of progressive encephalopathy in childhood. The Royal Army Medical College gave a lucid and comprehensive account of encephalitis, which was now the major cause of non-traumatic deaths among military personnel in the Far East. The department of psychological medicine, United Birmingham Hospitals, presented a very detailed account of prefrontal leucotomy, including historical background, experimental and neurophysiological rationale, method of selection of patients for the operation, and the end-results. The Institute of Neurology in London dealt with the carpal tunnel syndrome, with special emphasis on two new electrical tests of median nerve function developed to supplement clinical examination before and after treatment. A palmar fasciectomy was included in the colour television programme from the Queen Elizabeth Hospital on Wednesday, July 16. The Midland Centre for Neurosurgery, Smethwick, showed several new techniques for the detailed investigation of diseases of the lower motor neurone.

Medicine

Among the exhibits in the field of medicine, the Rheumatism Research Unit (of the Medical Research Council) at the Canadian Red Cross Memorial Hospital, Taplow, put on a challenging display concerned with the prophylaxis of rheumatic fever and the prevention of rheumatic heart disease. The Belfast City Hospital demonstrated the use of acetyl strophanthidin to determine digitalis requirement in congestive heart failure, while the United Birmingham Hospitals depicted disorders of electrolyte metabolism in this condition, with emphasis on low potassium levels. The Royal Victoria Hospital, Belfast, gave a comprehensive picture of Cushing's syndrome based on 16 cases, 13 of which were treated by subtotal adrenalectomy. The departments of medicine and surgery, Leeds University, combined to illustrate the place for medical and for surgical techniques in colitis. The value of cortisone and corticotrophin as well as of the topical application of hydrocortisone was amply demonstrated. Another demonstration of the way in which medical and surgical methods of treatment were complementary was in the management of tuberculosis of the urinary tract, as illustrated by the department of urology, United Birmingham Hospitals. The sole exhibit concerned with paediatrics was from the department of child health, University of Manchester: a tripartite display was devoted to pulmonary changes in acute glomerulonephritis of childhood, lung lesions in asthmatic children, and the relationship between vasomotor rhinitis and perennial asthma.

There were two booths dealing with dermatological subjects. The Walsall Group of Hospitals demonstrated beautiful three-dimensional models of sebaceous glands and discussed some of the changes seen in acne vulgaris. The M.R.C. Unit for Research on the Experimental Pathology of the Skin, United Birmingham Hospitals, and the regional plastic surgery centre, Wordsley Hospital, showed new methods for investigating the behaviour of skin and other tissues *in vitro*. They also presented a photographic demonstration of surgical techniques used in the treatment of radio-resistant skin cancer. Also in the field of malignant disease was the exhibition by the department of radiotherapy, United Birmingham Hospitals, of the value of radiotherapy in the treatment of malignancy. There was such a wealth of information at this stand as to justify a heading of "Multum in parvo." The value of exfoliative cytology in the diagnosis of neoplasms of the colon, bronchial tree, and female genital tract was well shown in a combined display by the departments of bacteriology, gynaecology, and surgery, United Birmingham Hospitals.

Surgery

Among the exhibits of surgical interest was one from the department of surgery, University of Birmingham—a colourful working demonstration of the Lillehei deWall heart–lung machine and its monitoring equipment as used for total cardiac bypass for open heart surgery. The treatment of hydronephrosis was dealt with by St. Peter's, St. Paul's, and St. Philip's Hospitals, the Institute of Urology, London, in a clearly illustrated exhibit, including photographs, drawings, radiographs, and cinepyelography studies on an editing machine. St. Bartholomew's Hospital and St. Thomas's Hospital, London, surgical professorial units, showed how *x*-ray and visual lymphangiography revealed specific defects in lymphoedema. Also of surgical as well as anaesthetic interest was the lifelike display by the department of anaesthesia, United Birmingham Hospitals, of the "Birmingham" hypothermia unit which surface-cools the patient by means of enveloping blankets, the temperature of which could be raised or lowered as desired. Visitors were able to see the unit in action for a craniotomy on the colour television programme on Friday, July 18.

The exhibit by the department of surgery, United Birmingham Hospitals, on peripheral vascular disease was of peculiar interest in that Joseph Hodgson, of Birmingham, who published a treatise on diseases of arteries and veins in 1815, had received international recognition for his pioneer work as a vascular surgeon. Modern clinical practices were demonstrated, and in addition peripheral arterial grafting was shown on the colour television programme on Monday, July 14.

The Institute of Ophthalmology, London, depicted the natural history of ocular herpes simplex, a disorder unaffected by antibiotics and in which the use of cortisone might be dangerous. The Royal National Throat and Ear Hospital, London, audiology unit, presented a clear account of a congenital deafness occurring as part of a hereditary syndrome, also characterized by a deformity of the inner angle of the eyelids, eyes of dissimilar colours, and a white forelock. The histological findings, shown here for the first time, indicated that the organ of Corti and the vestibular membrane were absent and that the density of the nerve fibres entering the cochlear canal was greatly reduced. One of the two booths devoted to dental surgery, that from the department of dental surgery, Queen Elizabeth Hospital, Birmingham, showed models and radiographs demonstrating methods of treating jaw fractures, and also many colour transparencies of oral conditions of medical interest. The School of Dental Surgery, Birmingham University, showed various aspects of their research work, including the application of isotope techniques for the examination of the hard dental tissues.

Of obstetrical interest was the exhibit from the National Maternity Hospital, Dublin, on the importance of haemolytic disease of the newborn. The indications for induction of labour and for exchange transfusion of the newborn child, and its technique, were shown in diagrams and posters of a high standard of professional signwriting. Near by, one facet of the problem—the use of liquor amnii studies in the prediction of this disease—was illustrated by St. Mary's and Park Hospitals and the department of medical illustration, Manchester Royal Infirmary. In this test the concentration of bilirubin in the liquor amnii is assessed by means of a spectrophotometer.

General Practice

The Midland Faculty of the College of General Practitioners illustrated epidemiology in general practice. One map showed the distribution of cases of epidemic bronchiolitis in children, the order in which they occurred being shown by the successive illumination of differently coloured light-bulbs. Other maps depicted the epidemiology of Bornholm disease and the distribution of cases of pernicious anaemia per 1,000 of the population.

The exhibit of the R.A.M.C. has already been noted. The R.A.F. Institute of Aviation Medicine showed a model of the laboratory in which research into thermal stress in flight is undertaken, while electro-medical instrumentation

[*Birmingham Post Studios*

The exhibit illustrating the use of radiotherapy in the treatment of malignant disease (the United Birmingham Hospitals, Department of Radiotherapy).

was displayed by No. 248 Maintenance Unit, R.A.F. The Royal Naval Air Medical School displayed equipment, including a helicopter, of air–sea rescue work and for survival at sea. The medical department of B.O.A.C. showed their equipment for the transport of seriously incapacitated invalids, as well as currently used oxygen masks and head-sets.

The Royal Hampshire County Hospital and Salisbury General Infirmary showed how a comprehensive rehabilitation service had been set up for the rural areas of the S.W. Metropolitan Regional Hospital Board.

Finally in the general section were two interesting displays. One was by the medical groups of the Royal Photographic Society and the Institute of British Photographers, London, illustrating new techniques in the more specialized branches of medical photography. In the other the Laboratory Animals Centre of the M.R.C. Laboratories, Carshalton, presented a very informative account of the different facets of their work and its importance to medical science.

An exhibition specially arranged for the meeting was that of the Pharmaceutical Society of Great Britain on the effect of formulation on drug action.

Awards of Merit

The displays were divided into two categories for the purposes of the judges. In the first category the award was for excellence of presentation, and the winning exhibit went to the department of radiotherapy, United Birmingham Hospitals (Mr. W. H. BOND and Dr. P. B. KUNKLER), for the display of the value and use of radiotherapy in the treatment of malignant disease. Two exhibits received honourable mention: (1) that of the audiology unit of the Royal National Throat and Ear Hospital (Dr. L. FISCH and Mr. D. J. CONNOLLY) depicting "Congenital Deafness as Part of a Hereditary Syndrome"; and (2) that of the Institute of Ophthalmology (Mr. BARRIE JONES and Dr. PETER HANSELL) depicting "Ocular Herpes Simplex."

In the second category the award was given for scientific merit and originality, and here the judges decided that two exhibits were equally deserving of first place. These were: "Disorders of Electrolyte Metabolism in Congestive Cardiac Failure" from the United Birmingham Hospitals (Dr. O. BRENNER and Dr. C. T. G. FLEAR), and "The Sebaceous Gland" from the Walsall group of hospitals (Dr. G. W. SENTER). The Midland Faculty of the College of General Practitioners' exhibit on "Epidemiology in General Practice" received honourable mention.

COLOUR TELEVISION AT BIRMINGHAM

The daily lunchtime programmes of colour television, sponsored and produced by Smith Kline and French Laboratories Ltd., were very popular with members and visitors to the Annual Meeting. The arrangements for the various programmes were made by Mr. W. H. BOND. Clinical demonstrations and surgical operations performed by members of the staff of the United Birmingham Hospitals in the Queen Elizabeth Hospital were shown in the Students Union to large and appreciative audiences, who appeared to approve of the medium for teaching and demonstration purposes. The impression made by some of the programmes was such that a few members of the audience had to be carried fainting out of the hall.

On July 14 Mr. A. J. H. RAINS demonstrated peripheral arterial grafting. On July 15 Mr. J. M. SMALL performed a hypophysectomy for breast cancer and Mr. A. GOUREVITCH showed intubation for inoperable growth of the cardia. The following day brought three items: palmar fasciectomy, by Mr. O. T. MANSFIELD; haemorrhoidectomy with suture, by Mr. B. N. BROOKE, and management of an ileostomy, presented by the Midlands Division of the Ileostomy Association. On July 17 Mr. A. L. D'ABREU demonstrated open cardiotomy. On the following day Professor BRODIE HUGHES, Mr. ERIC TURNER, and Dr. J. MCN. INGLIS showed craniotomy under hypothermia. In addition Dr. C. HAWKINS showed some medical rarities, and Dr. A. C. CROOKE and Dr. W. CANT illustrated dwarfism.

A specially pleasing feature of the television programmes was the use made of the medium in order to illustrate and amplify a number of the static displays in the Scientific Exhibition. This is a trend which is likely to persist, to the mutual advantage of demonstrators and viewers.

A surgical correspondent writes about the first programme on peripheral arterial grafting: Professor F. A. R. STAMMERS (Birmingham), in his introduction, briefly reviewed the history of the treatment of vascular disease. At the present time only one patient in ten with severe symptoms was suitable for replacement of a diseased artery with a graft. Mr. J. A. WILLIAMS (Birmingham) discussed the indications for grafting in greater detail. Patients might be divided into two main groups: those whose limb was in imminent danger, and those who had symptoms but no immediate threat to the limb. In the first group grafting should be attempted whenever possible; the decision was more difficult in the second category, because operation might make the patient worse in a proportion of cases. Mr. WILLIAMS and Mr. D. M. MORRISSEY (Birmingham) presented some patients who had been successfully treated; in one of them a large area of frank gangrene had healed after successful grafting. Dr. F. H. HOWARTH (Birmingham) demonstrated techniques of arteriography. He showed an ingenious modification of standard methods. An accessible artery was pierced with a trocar through which a soft metal guide was passed; plastic tubing was threaded over the guide after withdrawal of the trocar. Even the arch of the aorta could be readily demonstrated by this means after injection of radio-opaque dye. The televised operation by Mr. A. J. H. RAINS was on a 62-year-old man with a large popliteal aneurysm. After exploring the popliteal artery, Mr. Rains excised the aneurysm and successfully placed a long bypass graft from the superficial femoral artery to a normal region of the popliteal distal to the aneurysm. A homograft was used. Though the quality of the colour reproduction left something to be desired—swabs and instruments were bright blue, and blood appeared to be almost black at times—a good overall impression of the operation was obtained, though details of technique were seen only with difficulty.

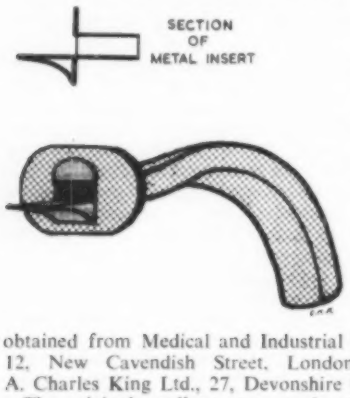
FILM SHOWS

Although screened at 5.15 p.m.—an hour when many had already had a full day—the film programmes attracted audiences of a fair size, and, at least on this occasion, the older medium seemed to be holding its own against television. A wide variety of films were shown, many of them combining medical and technical features of a high quality. Among the films shown were: "Management of an Ileostomy," by Bryan Brooke and United Birmingham Hospitals; "Special Equipment in the Education and Treatment of the Spastic Child," by A. Innes and Carlson House; "Caramels and Cavities," by Professor A. B. MacGregor; "Operation on Acromegalic," by Professor A. B. MacGregor; "Rehabilitation of a Double Leg Amputee," by Southend-on-Sea Hospital Management Committee; "The Doctor Defendant," by American Medical Association and American Bar Association; "Doctors' Hobbies Exhibition, 1957," by Benger Laboratories Ltd.; "Hypnotic Treatment of Psychogenic Illness," by N. M. Pai, St. Ebba's and Belmont Group Hospital Management Committee; "Postnatal Exercises to Prevent Stress Incontinence," by C. K. Vartan; "Bits and Pieces (Gynaecological)," by Professor C. S. Russell; "Life Goes on in Spite of Everything," by Dr. Tapani Kosonen, Aurora Hospital, Helsinki; "The Use of the Artificial Kidney," by R. Shackman, Postgraduate Medical School, London.

New Appliances

MODIFIED ANAESTHETIC AIRWAY

Dr. J. P. Kwella, of King's Mill Hospital, Sutton-in-Ashfield, Notts, writes: During inhalation anaesthesia with a rubber facemask and pharyngeal airway in place, a common and serious complication is for the lower edge of the facemask to ride up and obstruct the opening of the airway. A modification of the airway, shown in the drawing, prevents this. The metal insert has a ridge added to the lower edge of the opening, which stops the facemask from riding up.



The modified airway can be obtained from Medical and Industrial Equipment Ltd., 10–12, New Cavendish Street, London, W.1, or Messrs. A. Charles King Ltd., 27, Devonshire Street, London, W.1.

The original appliance was made with the help of Mr. L. Pembleton, surgical instrument technician at Harlow Wood Orthopaedic Hospital.

To-day's Drugs

In this column we publish from time to time authoritative notes on a selection of drugs in current use.

Delta-Cortelan (Glaxo Laboratories).—This substance is prednisone acetate, put up in tablets of 1 and 5 mg. It is some five times as effective as cortisone acetate, and the dosage is one-fifth that of the parent substance. Having in therapeutic doses less salt- and water-retaining effect than cortisone, prednisone is indicated in all those conditions in which cortisone is used except for Addison's disease and other adrenocortical deficiency states. In long-term therapy of rheumatoid arthritis it is wise not to exceed 15 mg. daily, as the incidence of toxic effects notably increases on higher dosage. Such toxic effects are the same as those seen with cortisone, though retention of sodium and water is considerably less.

N.H.S. basic price: 100 1-mg. tabs., 24s.; 100 5-mg. tabs., 100s.

Mepilin Tablets and Elixir (British Drug Houses, Ltd.).—Each tablet and each teaspoonful of elixir contains ethinyl oestradiol 0.01 mg. and methyl testosterone 3 mg. Other combined oestrogen–androgen preparations have varying proportions of the two ingredients.

The general idea underlying the combined use of oestrogen and androgen for the treatment of disorders due to deficiency of sex hormones is, firstly, that both types of hormone become deficient together; secondly, that there is a synergism in their anabolic effects; and thirdly that, because of this, the doses of either can be kept below the level at which side-effects might be produced. There is probably some truth in all this, though not enough to make the combined preparation invariably the one of choice. Thus, most cases of female climacteric syndrome are effectively treated by small doses of oestrogen alone; but it must be admitted that in the occasional difficult case the symptoms may be better controlled by the combined preparation, and the patient is less likely to have oestrogen-withdrawal bleeding when treatment is interrupted (as it always should be). Nevertheless, the amount of androgen in the preparation may be sufficient to cause hirsutism in some women, especially if more than one or two tablets a day are given.

Apart from the climacteric syndrome, oesteoporosis is an indication for combined oestrogen–androgen therapy, and there is some evidence that response is better than to oestrogen alone. For the inhibition of lactation the combined preparation would appear to have no real advantage over oestrogens alone.

N.H.S. basic price: 100 tabs., 12s.; 4 fl. oz. elixir, 6s.

Streptaquaine Solution (Distillers Company (Biochemicals) Ltd.).—This is a ready-prepared and stabilized sterile solution of streptomycin sulphate with phenol 0.5% added as a bacteriostatic agent. It is available in phials of 4 ml. (equivalent to 1 g. streptomycin base), 20 ml. (equivalent to 5 g.), and also in phials of 3 ml. (equivalent to 1 g.) and 15 ml. (equivalent to 5 g.). In addition 2 ml. cartridges are obtainable. These are equivalent to 1 g. of streptomycin base.

The preparation is for intramuscular injection only and is not suitable for intrathecal administration. It can be used for any of the conditions for which intramuscular streptomycin is a suitable treatment, particularly tuberculosis. The advantage is that the solution is already prepared and does not therefore have to be made up. Injections of streptaquaine solution are, like other stabilized solutions, a little more likely to give rise to pain than injections of freshly prepared solutions of streptomycin sulphate. In practice this difference seems to be of little importance.

N.H.S. basic price: 1 mega unit in 3 ml. or 4 ml., 5 phials for 7s. 6d.; 5 mega units in 15 ml. or 20 ml., 1 phial for 6s.

Albamycin GU (Upjohn of England Ltd.).—Each tablet contains novobiocin (as the calcium salt) 125 mg. and sulphamethizole 250 mg. This preparation is recommended for use in the treatment of urinary tract infections and in the prophylaxis of infection in patients with indwelling catheters.

Novobiocin is an antibiotic which is active against many Gram-positive and a few Gram-negative organisms. The best results are obtained in staphylococcal infections. Urticaria and sensitization dermatitis are somewhat frequent side-effects. Sulphamethizole is a rapidly absorbed and excreted sulphonamide which is relatively soluble. It has been used in low dosage with reported success in the treatment of urinary tract infections. There seems little justification for combining these two substances so as to provide a single preparation for use in urinary tract infections. The infecting organisms in the urinary tract are usually Gram-negative, and if they do not respond to sulphonamides full bacteriological study is necessary. Novobiocin is not a suitable substance for prophylactic use, since bacterial resistance develops fairly quickly and the patient is exposed to the dangers of sensitization reactions.

N.H.S. basic price: 100 tabs., 169s. 6d.

Ilotycin (Eli Lilly and Co. Ltd.).—Erythromycin in 100-mg. and 250-mg. tablets with acid-resistant coating. Erythromycin has a range of activity similar to that of penicillin. It has few toxic side-effects, but bacteria develop resistance to it at least as readily as they do to penicillin. It is active when given by mouth. Its main use is in the treatment of staphylococcal infections which have proved resistant to penicillin and other antibiotics. It is desirable that it should not be used indiscriminately so that there is no increase among the general population of strains of staphylococci resistant to it. Hence it should not be prescribed for trivial conditions, for chronic diseases, and where the bacterial cause is unknown. In practice this means that its use is best restricted to hospitals or to cases in which a staphylococcal infection such as a boil or septic finger has not responded to penicillin in full doses. It is especially useful in staphylococcal enteritis. It may be tried cautiously in patients who have become sensitized to penicillin. It is expensive.

N.H.S. basic price: 100 100-mg. tabs., 86s.; 100 250-mg. tabs., 185s. 8d.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Arresting an Outbreak of Poliomyelitis

SIR,—To those interested in the conquest of poliomyelitis the report by Dr. H. Koprowski and his colleagues (*Journal*, July 26, p. 187) must be hailed as a trial of great importance. It has for long been thought that feeding a community with attenuated strains of polio viruses would not only provide good protection but would arrest an epidemic safely, cheaply, and promptly.

This is apparently what has been achieved in the Belgian Congo, and this triumph must have important influences on the research programmes and vaccination policies of many countries.—I am, etc.,

Oxford. W. RITCHIE RUSSELL.

Prognosis of Cerebral Embolism

SIR,—I was very interested in the report from Mr. G. Keen and Dr. V. M. Leveaux on the prognosis of cerebral embolism in rheumatic heart disease (*Journal*, July 12, p. 91). In my own series[1] of 60 patients with cerebral embolism I find that in 36 this was associated with rheumatic heart disease, 31 having mitral stenosis with auricular fibrillation and 5 having mitral stenosis with sinus rhythm.

There is no doubt that the prognosis of this group of 36 patients was better than in the total group, where 50% of the untreated patients and 25% of those treated with anticoagulants died. The analysis of the rheumatic heart disease patients shows that in the untreated group of 21 patients five died, four were moderately disabled after five years, and 12 recovered. In the group treated by anticoagulants there were 15 patients, of whom one died, two were moderately disabled, and 12 recovered.

This supports the view generally held that the main prognostic factors of cerebral embolism are the age of the patient and the extent and completeness of the lesion, and this was further confirmed by the necropsy findings in the patients who died, where it was found in most cases that the occlusion was in one of the large cerebral vessels with extensive cerebral infarction as a result.—I am, etc.,

Ashford, Middlesex. A. BARHAM CARTER.

REFERENCE

1 Carter, A. Barham, *Quart. J. Med.*, 1957, **26**, 335.

Calcium and Phosphorus Metabolism

SIR,—As a general rule the diagnosis of hyperparathyroidism results from investigation of its complications, which may occur together or singly. At first the diagnostic complication was the classic bone disease of von Recklinghausen, but later stone formation in the urinary tract was shown to be more common.[1] More recently two further complications have been recognized, peptic ulcer[2] and pancreatitis,[3] and occasionally a psychosis may apparently result from the direct effect of hypercalcaemia. The association of hyperparathyroidism with other endocrine disease is also beginning to be known.[4] Disease of the parathyroid glands is being diagnosed more often, and the number of patients coming to operation at such centres as the Massachusetts General Hospital and the Mayo Clinic has increased markedly in the last decade. Hyperparathyroidism can no longer be considered to be a rare disease, but its diagnosis depends on accurate and repeated chemical estimations. Each hospital has to determine what are the upper limits of normal for its serum calcium estimations, and with experience this upper limit seems to fall. At the present time at the Massachusetts General Hospital, using the Fiske and E.D.T.A. methods, the upper limit of normal for a serum calcium reading is 10.6 mg./100 ml., and exploration has been carried out in patients with readings of 10.8 mg./100 ml. with success. At the Mayo Clinic the upper limit of normal is taken to be 10.3 mg./100 ml.[5]

In hyperparathyroidism the serum calcium level is not necessarily raised at all times and the disease appears to undergo cycles of activity. One normal serum calcium reading does not rule out hyperparathyroidism, but a raised serum calcium, with a lowered serum phosphate level and a 24-hour excretion of more than 150 mg. of calcium in the urine after an intake of 150 mg. or less calcium a day for the previous four days, is diagnostic (if metastatic carcinoma, sarcoidosis, myelomatosis, an excessive intake of milk and alkali, and hypervitaminosis D have been excluded). A lowered serum phosphate level below 3 mg./100 ml. is not invariably present,[6] and renal damage secondary to primary hyperparathyroidism may give phosphate retention and a low or normal 24-hour urinary excretion of calcium. Experience has shown that in some patients the renal function may improve after parathyroidectomy.

In the *Journal* for June 14 (p. 1385) Dr. G. L. Mouzas writes on "calcium and phosphate metabolic studies" in 85 patients with urinary calculi and discusses the diagnosis of hyperparathyroidism in these patients. He states the method used in estimating the serum calcium, and evidently takes 11 mg./100 ml. as the upper limit of normal. Only those patients with serum phosphate levels below 3 mg./100 ml., or with serum calcium levels above 11 mg./100 ml., had more than one determination carried out, and most of the first serum phosphate levels were apparently not taken following a period of fasting. Only few of the patients had 24-hour urinary calcium excretion tests. Dr. Mouzas states that no single test is satisfactory for parathyroid dysfunction and that only four of his 85 patients showed evidence suggestive of hyperparathyroidism. He does not state if any of the patients were explored nor which of the patients in Table III he considered to show evidence of hyperparathyroidism. Without further and repeated tests one cannot be certain, but in Table III at least 11 of the patients would appear to have hyperparathyroidism. It is doubtful, in fact, whether Dr. Mouzas has really screened his 85 patients for this disease.

The difficulties of diagnosis of hyperparathyroidism have already been stressed with some of the complications of this strange disease. A repeated raised serum calcium level still remains (in the absence of one of the conditions also giving hypercalcaemia and already mentioned) the one finding the most diagnostic of hyperparathyroidism. Hypercalciuria may be intermittent or absent despite the presence of renal stones; the serum level of phosphate is altered by the vagaries of diet and by kidney damage. At the present time the recently introduced tests of tubular reabsorption of phosphate[6] and renal clearance of phosphate[7] have not been fully assessed and the calcium infusion test of Howard[8] has proved disappointing.[6] These observations are based on the findings in over 200 patients at the Massachusetts General Hospital in whom hyperfunctioning parathyroid tissue was removed at operation.

There is a need for a more critical attitude to the diagnosis of hyperparathyroidism which will ultimately have to be judged on the results of operation. Until this is done many cases will be missed and hyperparathyroidism continue to be regarded as rare.—I am, etc.,

Boston, U.S.A. W. MILO KEYNES.

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Beds for the Aged

SIR,—Thanks to modern methods of treatment of tuberculosis the number of in-patients in sanatoria has been so drastically reduced that regional boards in Scotland are likely to put some of these sanatoria on a "care-and-maintenance basis" (*Hansard*, May 6, cols. 1013–14) I wish therefore to express my indignation and horror against this proposal—an iniquitous policy which I have no doubt

was prompted by the desire to save money. It is indeed most gratifying to know that the "White Man's Scourge" has at last been brought under control. But why in the name of humanity and common sense are these sanatoria to be allowed to be closed down? What about the thousands of old-age pensioners who are desperately in need of hospitalization?

If regional boards pursue this policy of closing down sanatoria and refuse to fill these beds with old people, then they must stand accused of callous indifference to the needs of old people. I therefore make a special appeal to my professional colleagues to rise as a body to support me in my campaign for more hospital beds for old-age pensioners. For who better than the family doctor is more familiar with the everyday human drama and appalling conditions under which the average pensioner lives and dies?

It is also a somewhat bitter and regrettable reflection on our noble profession that some doctors tend to show a complete indifference to the hospital needs of the elderly, as shown by the fact that these doctors too readily accept the reply when requesting the admission to hospital of an elderly patient: "Sorry, doctor, there is not a bed available. Your patient will be put on the waiting-list." What list, may I ask? The undertaker's list?—because many of them are dead or dying as the result of complications due to the delay before their turn for admission is reached. And for these deaths we, the medical profession, must also share in the guilt.

I sincerely hope this letter will be a challenge and inspiration to those members of the medical profession who by virtue of their position can and must do much more than they are doing at present for old people in times of illness; and at the same time act as a warning to the regional boards that old-age pensioners are also human beings and are equally entitled to the same rights and privileges as our younger patients in times of illness, and that obviously includes hospital beds.—I am, etc.,

Glasgow, S.W.3. ARNOLD B. COWAN,
Honorary Medical Officer,
Glasgow and West of Scotland Old Age Pensioners' Association.

Tattooing

SIR,—Recent correspondence concerning tattooing (see *Journal*, June 28, p. 1545) has failed to bring to light the tragic mutilation which is at present going on amongst juveniles, often below the age of 15. In the casualty department of this hospital one can expect to see two or three people each week of 15 or under who have been recently tattooed. Tragically these are not always young boys, but on occasion have been 15-year-old girls bitterly remorseful at the tattoo of some boy friend or well-known entertainer which they cannot erase from their forearms.

I have on several occasions tried to persuade the relatives of these people to take action against the tattooer, but the relatives have been reluctant to do this. Surely the tattooer cannot be allowed to disfigure a child in this manner when even a doctor may hesitate to set broken bones in a child of this age without the parent's consent.—I am, etc.,

Ancoats Hospital, Manchester, 4. DEREK BUNTING.

Ectopic Pregnancy after Pelvic Tuberculosis

SIR,—It was with considerable interest that I read the letter of Mr. Wilfrid G. Mills (*Journal*, July 19, p. 163) on ectopic pregnancy after pelvic tuberculosis. I have had a similar experience, having seen three cases of ectopic pregnancy during the last twelve months occurring in cases previously treated by me for pelvic tuberculosis, the only previous complaint of these patients being sterility. All three patients had apparently normal salpingograms on completion of treatment. One of these patients developed a paralytic ileus and very nearly died. Paradoxically the cure of the tuberculosis appears only to increase the subsequent hazards.

Whilst at the moment I would hesitate to advocate the removal of both Fallopian tubes from all women with pelvic tuberculosis, I have compromised to the extent of advocating a complete reassessment of each case at the end of twelve months' treatment, with a laparotomy and salpingectomy if one is at all doubtful, for the double reason of removing a tube which may still contain active tuberculosis and one which may be a source of an ectopic in the future. It may well be in the light of subsequent experience that routine removal of the Fallopian tubes may be necessary unless the patient is willing to run the risk of an ectopic for the very slight chance of conceiving. It is my opinion that the only patients who do conceive are those who are diagnosed in the very early stages of the disease or whose tubes are not affected.

The best course open to us is prevention by B.C.G., etc., and especially the use of antituberculous drugs in primary tuberculosis in young girls and women.—I am, etc.,

Galway, Eire. DIARMUID O'DRISCOLL.

Modified Mattress Suture

SIR,—The vertical or end-on mattress suture has obvious advantages in bringing together the deeper portions of the wound as well as approximating the skin edges. In obese patients, however, the skin edges occasionally tend to separate because there is no direct approximation as with a simple interrupted suture. To overcome this disadvantage, the following modification is suggested.

The vertical mattress suture is made in the ordinary way—the needle passes through the skin about half an inch or so from the proximal edge of the wound, and, taking a small amount of the subcutaneous tissue, emerges through the skin of the opposite (distal) side at the same distance. The edges of skin are held up by the suture material and the needle re-enters the skin on the distal side at a variable distance, depending upon the amount of subcutaneous fat, passes deeply, and emerges on the proximal side similarly. Before tying the two ends of the suture material together (as in the ordinary end-on mattress), however, the needle once again is passed through the loop on the distal side (see Fig. 1), and then with only moderate tension a reef knot

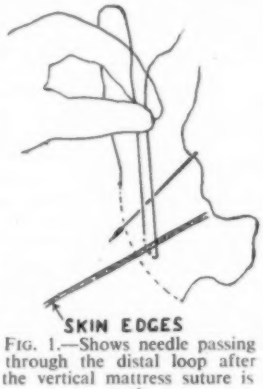

FIG. 1.—Shows needle passing through the distal loop after the vertical mattress suture is made.

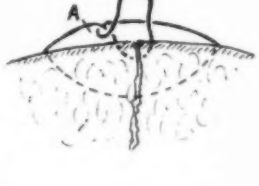

FIG. 2.—Diagrammatic cross-section of the modified vertical mattress suture prior to tightening. "A" is point of division for removal of suture.

is tied, preferably to lie on the distal side of the wound edge. The skin edges are thus nicely approximated, as also the deeper portions of the subcutaneous tissue, without undue tension.

The suture is removed in the usual way by pulling on the knot after cutting the suture material between its emergence and re-entry through the skin on either side (see Fig. 2). The removal is easier if the suture is cut on the side close to the knot.

I wish to thank my wife for the diagrams illustrating the suture.

—I am, etc.,

New Delhi, India. K. N. KASHYAP.

Wrong Connexions

SIR,—The letter from Dr. R. N. Sidebotham (*Journal*, July 19, p. 164) brings forcibly to mind a situation that I have envisaged for many a long day. The use of non-interchangeable connexions, safety colours, and even warning lights and signals on oxygen cylinders is having its effect in lulling the anaesthetist into a state of false security. In my student days my teacher, Dr. H. W. Featherstone, was always insistent that everything we used on a patient should be not only smelt, not only sniffed at, but tested by the administrator, and it has been my practice to do this always with equipment before any single general anaesthetic or hospital list, whether the equipment that is being used is the property of the hospital or myself. It has also been my custom always to teach this safety factor to students and postgraduates, and in my opinion to check everything oneself is the least one can do when one is carrying the life of one's patients in one's hands. No precautions taken by the anaesthetist can be regarded as either "pedantic" or unnecessary in the circumstances.

I do not wish the impression to be created that I am against the safety methods that have been adopted by the manufacturers of anaesthetic equipment; in fact I am all in favour of them, and was one of the first to draw the attention of the manufacturers to the necessity for doing this on pipe-lines in the very early days of the war. I do, however, feel that safety measures on the part of the manufacturers do not mean that the anaesthetist must get slack and complacent about the equipment he uses, and the same vigilance is necessary to-day as it was before the introduction of these safety measures. I have myself seen a maintenance engineer fix a blue ferrule on the end of an oxygen pipe-line; consequently it is essential that anaesthetists must be constantly on their guard that the human element has not crept in to produce errors prior to their use of the equipment provided.—I am, etc.,

London, W.1. VICTOR GOLDMAN.

Psoriasis of the Mouth

SIR,—I read with interest Drs. R. P. Warin, H. S. M. Crabb, and A. I. Darling's paper "Lichen Planus of the Mouth" (*Journal*, April 26, p. 983) and noted one case suffered from psoriasis. Is it not possible that the mouth lesions were psoriatic? Psoriasis of the mouth is not common, but cases have been reported.[1]

During the past year I have seen two cases of psoriasis of the mouth. The first at the Australian Dermatological Congress, when the patient had psoriasis and a dusky mottled erythema of the palate. This case was confirmed by histopathology. My own case had generalized psoriasis with white plaques on the buccal mucosa and dusky erythema of the palate and fauces. The biopsy in this case was inconclusive, but the trouble cleared contemporaneously with the skin rash. I would be most interested to read of any similar observations.—I am, etc.,

Newcastle, Australia. W. W. GUNTHER.

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Pregnancy Cravings

SIR,—I was interested to read the article by Mr. J. M. Harries and Mr. T. F. Hughes about the "cravings" of pregnant women (*Journal*, July 5, p. 39). The authors mention the possible physiological or psychological origin. I suggest that they may also find relevant a neurophysiological approach in Pavlovian terms.

The tendency for such cravings to be more marked in early pregnancy suggests an adaptational problem, and it passes as the body accommodates to the pregnancy. An increased response to food is usual and leads to the building up of reserves. That this adaptation is stressful to the nervous system, as change so often is, is shown by the pathophysiological ultraparadoxical responses, where categories of substance resembling "food and drink" but definitely not "food and drink" are responded to as if they were food and drink (Table III), and on the other hand the normal responses to food and drink are inhibited so that substances normally liked are rejected in pregnancy (Table IV). This inhibition may merely manifest itself as a disinclination to eat or may be more severe as in nausea and sickness of pregnancy (assuming simple reflex vomiting from the uterus does not always account fully for the latter). This illustrates well the reversal of the differentially associated paired systems based on the feeding reflex function, and the pathophysiological nature is further emphasized by the compulsive force of the behaviour, the specificity of the responses, the need for secrecy, and the shame experienced, for the behaviour is so contrary to training. This does not explain the behaviour but it carries the problem of explanation into the central nervous system and a full causal explanation would require to answer the question, "How do ultraparadoxical responses arise in pregnancy?"—I am, etc.,

Gartcosh, Lanarkshire. W. W. GORDON.

Prostatitis and Ankylosing Spondylitis

SIR,—Apart from congratulating Dr. R. M. Mason and his associates for their thorough research on this subject as published in your issue of March 29 (p. 748), I would like to comment on the discussion and summary.

I do not think there is any doubt about their conclusion "that there is a real association between ankylosing spondylitis and inflammatory disease of the urogenital tract." But they do not elaborate the point that the inflammatory disease might be a non-infective inflammation. They do not appear to consider the possibility of inflammation of either the joints or prostate being caused by some mechanism other than microbial, although one of their sentences could be interpreted along these lines: "Conversely, the cause of the prostatitis may be a single one which operates to produce sacro-iliitis only in those patients with a suitable genetic background." However, as the authors have not developed this interpretation of the data presented, I propose to elucidate the matter.

Inflammation in any organ is essentially the end result of a certain pattern of arteriolar dilatation. The arteriolar dilatation results in *dolor, rubor, calor, tumor,* and *functio laesa* of varying degrees. The same inflammatory phenomena can result from many agencies: trauma (physical, chemical, or irradiational), infection, or the toxins from infective organisms can all produce the necessary arteriolar pattern, via the autonomic nervous system. Over the past half-century inflammation has become inseparably associated with infection in the medical and lay mind. Yet a moment's reflection establishes that infectious inflammation occupies a place altogether out of proportion to its actual incidence. Till recently the greatest number of cases of inflammation in this city were dermatitis *ab solare* (surfing season), and only a small proportion of them develop secondary infection. Tissue damage has initiated the arteriolar pattern of inflammation.

As in all cases of inflammation, the arteriolar pattern, and other defence reactions, are mediated by the autonomic nervous system under the regulation of the diencephalic nuclei generically grouped as the hypothalamus. Through a malfunction of this system—autonomic dyspraxia—the localized arteriolar pattern of inflammation can occur peripherally, causing a type of inflammation other than traumatic or infective. This mechanism accords with the term neurodermatitis as applied to certain idiopathic skin inflammations. It has been shown elsewhere in greater detail[1] that this pathological process is not confined to the skin. As one would expect, this autonomic inflammation may occur in any organ with an autonomic supply. In the present case the possibility has to be considered that the ankylosing spondylitis and the associated prostatitis are non-infective inflammations of the same autonomic nature, resulting from a common cause. There is evidence to show that the common factor is autonomic dyspraxia, which by

definition is an unstable state of the autonomic nervous system, caused from central overloading of the hypothalamus by an emotional crisis and resulting in peripheral malfunction of plain-muscle fibre or gland. In these cases the plain-muscle fibres concerned would be the media of the articular arteries and the prostatic blood vessels, the sacro-iliac joints and the prostate sharing a common or contiguous segmental supply as regards autonomic activity.—I am, etc.,

Sydney, Australia. BRIAN HAYNES.

REFERENCE

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Hazards from Cosmetics

SIR,—In your annotation on hazards from cosmetics (*Journal*, July 5, p. 38) you draw attention to the occurrence of dermatitis of the hands apparently caused by the synergistic action of household detergents and triethanolamine in a hand lotion. In this connexion it is noteworthy that a recent report of the Barrier Substances Sub-Committee of the British Pharmaceutical Codex Revision Committee[1] has produced a series of formulae, three of which contain triethanolamine salts. Particularly, their formula for a water-repellent barrier cream contains triethanolamine stearate, and it is clear that this formula is most likely to be used in conjunction with synthetic detergents under both domestic and industrial conditions. It would appear that the hazard is at its maximum with a barrier cream intended to be applied before work rather than a hand-conditioning preparation, since in the former case the detergent and triethanolamine will be present together in the skin for the maximum time.—I am, etc.,

London, N.W.1. K. B. ALBERMAN,
Technical Director,
Scientific Pharmacals, Ltd.

REFERENCE

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"Stelazine" in Psychiatry

SIR,—We were surprised to read the conclusions reached by Dr. M. E. Forrester following her trial of "stelazine" (*Journal*, July 12, p. 90). For the past eight months we have been carrying out an extensive controlled trial of this drug, the preliminary results of which are shortly to be published, and have found it to be extremely useful, not only for chronic psychotics but also in cases of more recent onset, and in particular we have had some striking results in the paranoid group of psychoses. Although we also found some side-effects, these seldom occurred on dosage of 10–20 mg. a day, which we concluded was the maximum dose necessary for therapeutic effect in most cases.

Far from condemning stelazine, we would say that it is one of the most powerful and effective of the recent spate of drugs available for the treatment of psychiatric cases and suggest that further carefully controlled trials will prove its worth.—We are, etc.,

Epsom. J. R. A. MADGWICK.
D. L. MCNEILL.
MARIE DRIVER.

SIR,—I am somewhat concerned to read the account of a "pilot trial" of "stelazine" reported by Dr. M. E. Forrester (*Journal*, July 12, p. 90). The results of an uncontrolled series of only 25 cases receiving treatment for a period of four weeks may reasonably lead to the doctor in charge of a ward making certain assumptions and deciding that the patients of that particular ward should no longer have this form of therapy. It must be obvious to anyone with a scientific training that these conclusions have no wider validity whatsoever.

Approaching the subject objectively, the same drug, i.e. stelazine, has been tested in the hospitals of the St. James and Portsmouth Groups. Having been favourably impressed by the results in a properly controlled series of 60 patients (using the double blind technique), and having continued the treatment over a period of several months, we have by now used this drug with good results in approximately 200 patients. Despite the fact that our trial has been in progress for over six months, we realize that, at present, no definite scientific conclusions are possible, but our clinical impression is entirely contrary to that of Dr. Forrester. Except in mental defectives, in whose case the drug may possibly be contraindicated, we have experienced no serious side-effects, provided the dose is slowly increased, and we have found that symptoms of Parkinsonism rarely occur when a dosage not exceeding 25 mg. per day is used. It is seldom necessary to give more than 30 mg. per day. In our experience, stelazine is surprisingly free from the unpleasant side-effects of other phenothiazine compounds.

One can only regret the publicity given to severe adverse criticism of a new drug and unwarrantable conclusions based on a totally inadequate investigation which does not permit of scientific evaluation.—I am, etc.,

Portsmouth. W. LIDDELL MILLIGAN.

Delivery of the Placenta

SIR,—I have read with interest the report of Mr. Norman Kimbell's paper on the Brandt–Andrews method of delivery of the placenta, read to the Section of Obstetrics and Gynaecology at the Annual Meeting (*Journal*, July 19, p. 155). May I suggest that it was the improved recognition of the signs of separation of the placenta consequent on the local enthusiasm and study of a new method of management of the third stage that led to the excellent Peterborough results, rather than the precise method of delivery?

In my own experience in general and hospital practice I have found that the third stage rarely exceeds eight minutes even when ergometrine has not been given at the end of the second stage. I attribute this finding to the fact that I always use the dorsal position for the delivery of the child. Failure to recognize that separation of the placenta has occurred leads to many post-partum haemorrhages, particularly when a small lip of placenta has been caught in the cervix. This non-recognition is often due to the difficulty of feeling the uterus in the lateral position. By the time that the mother has gone through the messy and uncomfortable business of being lugged on to her back, and the infant has been put in a safe place, the placenta has separated. But as the uterus either has been palpated inadequately or not at all in the lateral position the signs of separation are not recognized. The attendant then waits 15 minutes, or whatever magic period he or she has been taught at their training school, and then "has a go." It is this uncertainty that leads to post-partum haemorrhage as much as the behaviour of the uterine muscle.

In the same issue of the *Journal* (p. 138), Mr. Mostyn P. Embrey and Mr. William J. Garrett add further proof of the speed and uniformity of action of ergometrine when given intravenously. Surely the realization of the efficacy of ergometrine when given by this route is the greatest advance in obstetrics in the past 10 years. Isn't it therefore about time that midwives were trained and allowed to use it in this way in the treatment of emergency post-partum haemorrhage?—I am, etc.,

Ingatestone, Essex. JOHN BURY.

SIR,—With the disclosure of many magic methods of removing the placenta, the importance of emptying the bladder may tend to be overlooked. I have tried the "new" method of cord-traction twice, successfully the first time, but after discharge the woman was readmitted in a state of shock from haemorrhage due to a retained segment. In the second case the refinement of amyl nitrite was added, but the cord broke, and manual removal of a placenta in the fundus was made difficult by a strong constriction ring. No ergometrine had been given.—I am, etc.,

Ba, Fiji. D. R. LITHGOW.

Lymphoedema

SIR,—I was very interested in the paper on the protein content of oedema fluid in lymphoedema by Mr. G. W. Taylor, Professor J. B. Kinmonth, and Dr. W. G. Dangerfield (*Journal*, May 17, p. 1159).

The results of a small series of electrophoretic analyses of fluid from cases of elephantiasis due to *Wuchereria bancrofti* may be of interest. The analyses were made on an Antweiler electrophoresis apparatus by Miss M. Lyle, B.Sc., and the results were as follows:

	Total Protein	Alb.	Glob.	A./G. Ratio
1 Elephantiasis of leg:				
(*a*) Fluid from top of leg ..	2·24	0·76	1·48	0·51
(*b*) Fluid from bottom of leg ..	2·82	1·05	1·77	0·59
2 Elephantiasis of scrotum (23½ lb. —10·7 kg.), 8 years	4·25	1·08	3·17	0·34
3 Elephantiasis of scrotum (3½ lb. —1·6 kg.), 6 years	2·84	0·28	1·56	0·82
4 Elephantiasis of scrotum (9 oz. —0·26 kg.)	2·92	1·09	1·83	0·59
Serum	6·28	2·0	4·28	0·46
5 Elephantiasis of scrotum (? wt.) ..	2·61	1·40	1·21	1·16
Serum	6·96	2·35	4·61	0·51
Mean of oedema fluid	2·94	0·94	1·84	0·67
Mean of sera	6·62	2·18	4·45	0·49

Parallel analyses of sera were made in only two of the cases (4 and 5), but they both illustrate the inverse A./G. ratio typical of the African,[1] and this is reflected in the A./G. ratio of the tissue fluid. In spite of this the total protein in this series is almost the same as in the series of Mr. Taylor and his colleagues (2.8 g.). The γ fraction formed the bulk of the globulin in the tissue fluid and was no doubt derived from the high γ globulin found in African serum. The high protein content in the fluid from the large, 23½ lb. (10.7 kg.) scrotum—said to be of eight years' duration—agrees with Crockett's finding[2] of high values when the disease is of long duration. The finding—admittedly in only one case—of a higher protein value at the bottom of the leg compared with that at the top (case 1 (a) and (b)) does not agree with Crockett's finding. It does, however, appear reasonable to expect a gradual diminution in the high protein content of the diseased tissue to a normal value in the unaffected tissue. Excluding the 4.25 g. value for the large scrotum, the range in the other cases is very limited and would appear to fit Crockett's idiopathic lymphoedema group of oedemas better than the lymphatic interruption group into which he has placed filarial elephantiasis.

The findings in elephantoid fluid are very different from those in filarial hydrocoeles. In these cases an A./G. ratio of 1.48 (16 cases) was found in spite of the inverse A./G. ratio in the serum, and the total protein in these cases of 4.2 g. per 100 ml. is identical with the value obtained by Crockett in a case of acute generalized allergic oedema. It is hoped to publish details of the findings in these cases later.—I am, etc.,

Mwanza, Tanganyika. P. JORDAN.

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[1] Holmes, E. G., Stanier, M. W., Semambo, Y. B., and Jones, E. R., *Trans. roy. Soc. trop. Med. Hyg.*, 1951, **45**, 371.
[2] Crockett, D. J., *Lancet*, 1956, **2**, 1179.

Pertussis and Tetanus Immunization

SIR,—There are two letters in your issue of July 26 which seem to require comment. The first is from Drs. D. C. Thursby-Pelham and C. Giles (p. 246), in which neurological complications following pertussis immunization in six children are described. This is a disturbing matter, and one is tempted to wonder whether the medical men who performed the injections made those preliminary inquiries which I personally consider essential. These are, in short, to make certain that the child has never had a fit or convulsion, and that there is no near family history of this; then that the child has not been near any infectious disease recently, e.g., poliomyelitis; finally, that there is no near family history of allergy, e.g., asthma or eczema.

Using this history as a guide to the suitability of the subject for pertussis inoculation, in a very considerable experience, I think I have been lucky enough to encounter nothing worse than drowsiness, pyrexia, or marked restlessness in an occasional case. There is no doubt that many doctors give these injections without taking the precaution of asking about the family history, etc. Also I do think that samples of pertussis vaccine from different sources show marked variation in their liability to produce reactions. On the whole, I have found the Wright–Fleming product fairly satisfactory in this respect. It may be that I have been lucky in avoiding more serious reactions; it may even be that I have not heard about them, for, in every hundred babies which one starts to immunize, a few fall by the way and do not complete the course, and the reason is often unknown, though moving from the locality without informing the health authority is one frequent cause. I would stress, however, that doctors undertaking this work should be made aware of the necessity of obtaining a careful history before just casually injecting 20,000 million *Haemophilus pertussis* into a child.

The letter by Dr. P. Jackson (*Journal*, July 26, p. 249) on the subject of tetanus immunization only serves to underline a plea which I have frequently made. When a child has received three injections of tetanus toxoid at my hands, usually in combination with diphtheria toxoid and *H. pertussis* vaccine, the parent is given a certificate which is boldly stamped "ALSO TETANUS," and told that, in the event of the child being taken to hospital with a wound or as the result of an accident, the certificate should be produced at once to the hospital authorities. It seems as if this may not be the procedure in Liverpool. Even if the public health authorities do so advise, it may be that private practitioners do not, and this necessity should be made clear to them. After all, the main object of tetanus immunization is to prevent the indiscriminate use of anti-tetanic serum.—I am, etc.,

Broadbridge Heath, Sussex. GUY BOUSFIELD.

Pseudo-medical Advertising

SIR,—As Dr. Dick Glover points out (*Journal*, July 19, p. 165) the public often prefer to buy tonics, vitamins, painkillers, and indigestion remedies for themselves, rather than go to the doctor to see if they need them. Vitamins especially, and tonics very often, are not indicated at all, while many a person suffering from a peptic ulcer "cures" his indigestion for himself until the ulcer perforates.

The public should spend its money as it likes, but its credulity where health is concerned should not be played on for purely business interests.—I am, etc.,

London, N.19. T. C. DANN.

Deluge of Advertisements

SIR,—Our practice, consisting of three partners, this morning received 23 circulars from pharmaceutical firms. Is this a record?—I am, etc.,

Liverpool, 8. B. JOHN MAXWELL.

Doctors' Book-plates

SIR,—Some years ago, when working in Great Britain, I started to collect doctors' *Ex Libris* book-plates. My idea was to compile these into a book of doctors (in Great Britain) and their book-plates. Similar books have been published in Holland and elsewhere. However, when I left England this work was temporarily stopped, and I am now commencing again.

Should any doctor wish to have his book-plate included in my book, I should be very grateful if he would send me two copies of his book-plate, with his name and address, and also an explanation of the symbolism of the book-plate. Due acknowledgment will be made in each case.—I am, etc.,

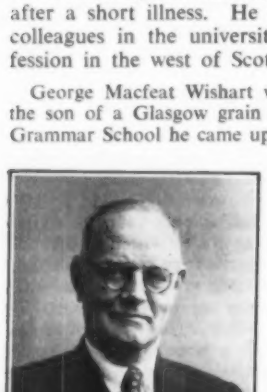
903 Medical Centre, Heerengracht, Cape Town. MAURICE NELLEN.

Obituary

G. M. WISHART, M.D., B.Sc., F.R.F.P.S.

Professor George M. Wishart, professor of applied physiology in the University of Glasgow, dean of the faculty of medicine and director of postgraduate medical education, died on July 18 in his sixty-third year after a short illness. He will be sadly missed by his colleagues in the university and by the medical profession in the west of Scotland.

George Macfeat Wishart was born on August 18, 1895, the son of a Glasgow grain merchant. From Uddingston Grammar School he came up to Glasgow University before the first world war and first graduated in science in 1916: he took his M.B., Ch.B. two years later. Thereafter he saw service with the medical branch of the R.A.F. In 1919 he returned to his university, which he was to serve in several capacities for the succeeding 39 years. He proceeded M.D., with honours, in 1926, and was elected F.R.F.P.S. in 1940. For two years Wishart was an assistant lecturer in the physiology department, and then in 1921 he became Grieve lecturer in physiological chemistry. This lectureship he held until 1934, when, for one year only, he returned to the physiology department as lecturer. In 1935, however, he returned to his real love and was appointed to the Gardiner chair of physiological chemistry. In 1947 Wishart resigned this chair to become director of postgraduate medical education: he was also dean of the medical faculty and professor of applied physiology. Appointed a member of the General Medical Council in 1947, he was also a member of the Scottish Health Services Council and of the General Nursing Council for Scotland.



[Annan, Glasgow

R. C. G. writes: It is doubtful if in the future any one individual will be able to profess both physiology and biochemistry. But Wishart could and did with success. His basic academic training was in the physical sciences, and he capped that with experience of the finest of all biological disciplines, the medical curriculum. From this, no doubt, he derived his sympathetic understanding of human beings, colleagues and students alike.

At a time when the majority of medical men had little chemistry and less physics, Wishart was thoroughly at home in these subjects. He enjoyed the application of exact methods to the problems of physiology and of biochemistry; the outcome could not fail to be rewarding. Wishart studied oxidative processes and worked on some chemical aspects of metabolism, but his real love was indirect calorimetry of human beings: he had to use the Douglas bag and Haldane's gas-analysis apparatus, and his skill with the latter was the envy and despair of his colleagues. His M.D. thesis was on "Basal Metabolism," and he was awarded a Bellahouston Gold Medal. About this time the use of statistics to treat results was in its infancy: here again Wishart was in his element. Again electronic devices were developing rapidly, and Wishart, instead of resisting such developments as so many of his colleagues did, accepted the innovations with understanding and contributed to their development and extension.

The appointment to the chair of physiological chemistry, and academic administrative duties in general, began to interfere with Wishart's personal participation in research. The later assumption of the onerous duties of postgraduate dean in the post-war years finally severed his connexion with the laboratory, although he was always a welcome and honoured visitor in his old haunts. The problems of medical education and of the National Health Service demanded all of Wishart's time—indeed, more time than should be asked of any one individual. Wishart conducted his administrative affairs with great care and with scrupulous fairness to all the interests concerned. He spent his days in helpful and friendly consultation with his staff and colleagues; his evenings he spent alone marshalling and collating the results of the past day's deliberations. He was indeed a man dedicated to the service of his university and of his profession.

Much of the early classical work on the expenditure of energy by women in various physical tasks was carried out by Elizabeth M. Bedale in the Glasgow physiology laboratories. Wishart and Miss Bedale were married in 1926. Our deepest sympathy goes out to the widow and to the two daughters of the marriage, one of whom followed in her father's footsteps, training first in science and then qualifying in medicine.

Dr. A. K. BOWMAN writes: More than ten years have passed since Professor Wishart became a member of the Western Regional Hospital Board. He was—if we may use the expression—one of the founder members; and of that pioneering company there now remains but one in active membership. We mourn, in the death of Professor Wishart, the loss of a colleague, counsellor, and friend who through his presence added dignity and power to the deliberations of the board. To the board, as to the many other causes with which he was associated, he gave the most single-minded and self-effacing service. I know of no one who, in his capacity as a board member as well as that of dean of the medical faculty and director of postgraduate medical education in the University of Glasgow, has approached so closely to the title of the irreplaceable. In his earlier years Professor Wishart was devoted to the development of certain phases of the scientific medicine which we know to-day; but his instincts and attitudes were so humanitarian that he combined in his own person the virtues of the pure scientist with the arts which characterize the true physician. Later he was to become an expert in treading the thorny paths of the administrator. Quiet and painstaking, rich in sympathy, compassionate, gentle of habit, just, resolute, and humble in the face of nature and of human personality, he poured out the last full measure of devotion to his many duties. His memory will continue to quicken and inspire those who for many years have looked to him for guidance and encouragement; and I know how deep must have been the springs from which such influence could flow.

H. B. WILSON, M.B., F.F.A. R.C.S., D.P.H.

Dr. H. B. Wilson, consultant anaesthetist to the Aberdeen Royal Infirmary and director of anaesthetic services under the North-eastern Regional Hospital Board (Scotland), died on July 3. His death, after a brief illness, came as a shock to his medical colleagues and to a host of friends and old patients. He was only 50 years of age, and in the previous week had been engaged in his work as usual with no hint that his life was to come so soon to its end.

Howard Bruce Wilson was born on November 20, 1907, the son of Dr. E. B. Wilson, a graduate of Aberdeen University, then in practice in Sheffield. He was educated at Aberdeen Grammar School and at Aberdeen University, where he gained many academic distinctions, and graduated M.B., Ch.B., with honours, in 1930. After graduation he engaged in general practice in London and then studied for, and obtained, the D.P.H. at London University in 1932. During the succeeding years he became more and more interested in anaesthetics and decided to make this his life's work. He was appointed honorary anaesthetist to the Bolingbroke Hospital in 1939, and in 1940 took the D.A. of

the English Royal Colleges. From 1941 until the end of the second world war he served with the R.A.F. Medical Branch, at first at home and, from 1943, overseas, as senior anaesthetic specialist to the R.A.F. British North African and Central Mediterranean Forces, attaining the rank of squadron leader. He carried his keen interest in the R.A.F. and in aeroplanes into civilian life, possessed his pilot's certificate, and used to fly frequently.

On demobilization Dr. Wilson was appointed honorary assistant anaesthetist to the Royal Aberdeen Hospital for Sick Children and to the City and Woodend hospitals, becoming senior anaesthetist in 1947. From the inception of the thoracic surgery unit, also in 1947, he undertook the organization of its anaesthetic service and the training of the anaesthetic staff. With the coming of the National Health Service in 1948, he was appointed consultant anaesthetist to the North-eastern Regional Hospital Board (Scotland) and, in 1954, senior anaesthetist and lecturer in anaesthetics to the University of Aberdeen. When the British Medical Association held its Annual Meeting at Harrogate in 1949 he served as a vice-president of the Section of Anaesthetics. In the previous year he was elected to the Fellowship of the Faculty of Anaesthetists of the Royal College of Surgeons of England. He served as a member of the council of the Section of Anaesthetics of the Royal Society of Medicine and of the Association of Anaesthetists of Great Britain, attending the meetings of these bodies with exemplary regularity, and paying frequent visits to numerous clinics in this country and to hospitals abroad—in France, Heidelberg, and Copenhagen—to further his knowledge of advances in his subject. He was associated with the editorial board of *Excerpta Medica* and contributed many abstracts to that and to other journals. His research work was mainly clinical, being concerned with the trial and assessment of anaesthetic drugs before their release for general use, and several papers were published. At the invitation of the joint anaesthetic committee of the Medical Research Council and the Royal Society of Medicine, he carried out a research on one of the curare derivatives.

S. G. D. writes: Howard Wilson's main interest in life, outside his family, was his profession. Born a perfectionist, he was bred a doctor. His sense of dedication was compelling, and although for many years not in robust health, and often laid aside by illness, he never spared himself in the service of his profession or of mankind. No call for help went unanswered, by day or by night, in fair weather or in foul. His aim was to supply the best possible anaesthetic service to the community, and to achieve this he drove himself to the limits of endurance and threw every reserve into the fight. He was an excellent doctor and a most expert anaesthetist, calm, kindly, and quietly but clearly in control, the possessor of the confidence of patient and colleague. With him at the top of the table, one knew that all was well, that all would be done that could be done to make the anaesthetic safe and satisfactory and the post-operative course smooth. The best index of the confidence and regard in which he was held by his colleagues is the great number of them who, coming to operation, chose him as their anaesthetist. As a teacher and trainer he was excellent, taking infinite pains with the honest trier, and inspiring the young members of his staff by his example to give the best of which they were capable. His single-minded devotion to the highest ideals of his profession in word and deed, and his mastery of his craft, are his enduring memorials. That he should be struck down at the height of his powers is a cruel loss to medicine, and an impoverishment of the whole community in which he lived and worked. It is difficult to realize that the ardent spirit has burned out and that the skill and wise counsel of Howard Wilson will not be there when next they are wanted. Friendly, considerate, warm-hearted, and generous, he attracted friends from all walks of life and held them by his sincerity and loyalty and by the feeling that here was a man one could admire and at all times trust. He was an enthusiastic flier and motorist, and greatly enjoyed organizing or taking part in a rally and talking about engines and their accomplishments. To his widow, his son, and daughter, and to his father, our deep sympathy goes out in their bereavement.

M. B. Y. writes: Those anaesthetists who at some time in their career spent a period of training under Dr. Howard Wilson's guidance owe him an especial debt. His teaching of anaesthesia in all its branches was invaluable, but above all he will be remembered for the help he gave in the specialty of anaesthesia for children. He came readily to the assistance of those less able than himself at any hour of the day or night, armed with dexterity and knowledge. His warm and friendly personality made him always approachable, and no problem was too trivial for his consideration. His unfailing cheerfulness, advice, and practical skill will be sadly missed by colleagues, patients, and friends, and the many who miss him offer their deepest sympathy to his widow, son, and daughter.

P. V. ANDERSON, M.B., B.S.

Dr. P. V. Anderson, who was a well-known general practitioner in County Durham and one of the first members to be admitted to the Roll of Fellows of the British Medical Association, died at his home at Shildon on July 5. He was 65.

Percy Vernon Anderson was born at High Grange, Bishop Auckland, on March 21, 1893. From Barnard Castle School he went on to the College of Medicine, Newcastle upon Tyne, but like many other students gave up his studies to join the Army at the beginning of the first world war. But in 1915 he was sent back to complete his medical training, and he graduated M.B., B.S.(Durham) in 1917. After holding the posts of house-surgeon and house-physician at the Royal Victoria Infirmary, he returned to the Army and served as a captain in the R.A.M.C. in East Africa. In 1919 he began practice in Shildon, where for the last twenty years he was also part-time medical officer of health to the urban district council and medical officer to the Shildon and District Infectious Diseases Hospital. He was also in charge of the geriatric patients at the hospital.

He took a keen interest in professional affairs and was a tireless worker for the B.M.A. From 1925 to 1947 he was honorary secretary of the Bishop Auckland Division and represented his Division at a number of Annual Meetings. Elected to the Durham County Insurance Committee in 1928, he was its chairman in 1948, when it became the executive council, and was then vice-chairman until 1951. After having been a member of the Durham panel committee he was chairman of the local medical committee from 1948 to 1958. From 1930 to 1951 he was a member of the Insurance Acts Committee—later the General Medical Services Committee—and from 1948 to 1958 a member of the Medical Practices Committee. He was a member of the Medical Planning Commission set up by the B.M.A. in 1940, and just before his death he was elected to the Roll of Fellows of the B.M.A.—a fitting distinction for his outstanding services to the Association.

F. R. writes: Despite the great amount of committee work he undertook, P. V. Anderson remained keenly interested in clinical medicine. He was a shrewd clinician and a good doctor who conducted a large practice with kindness and skill. Because of this devotion to clinical work his counsel on committees was even more valuable. His advice was constantly sought by many doctors on personal and practice problems, and his opinion was respected and always worth having. A man of sound and careful judgment, he was very modest and was never known to boast of anything. He had a keen sense of fun and a dislike of pomp and unnecessary fuss. His main attribute was his immense fund of common sense. He represented a type of doctor who in his devotion to his patients and his profession is one both patients and colleagues will sadly miss. His home life was very happy, and to his wife, son, and two daughters—the son and one daughter both in medicine—we extend our sympathy.

F. C. HOYTE, M.B., B.S., F.R.C.S.

Mr. F. C. Hoyte, surgical registrar at the Liverpool Thoracic Unit, lost his life on July 7 when climbing in the Karakoram range of the Himalayas. He was 32 years of age.

Dr. W. K. PALLISTER writes: On July 7 at about 11 in the morning Frank Christopher Hoyte and his expedition leader, Edward Warr, were last seen on an ice ridge which leads, only three hundred feet above, to the summit of Mount Minapin, in the Karakoram. Success seemed within their grasp, when heavy cloud covered the mountain and a high wind rose. Three hours later, when the weather cleared, the two climbers were no longer to be seen. A search revealed only their tracks up to the ridge, and it must be presumed that they had fallen from the mountain face and been killed.

Chris Hoyte was born on May 28, 1926, in the Belgian Congo, where his parents were medical missionaries. His childhood was spent in Northern Rhodesia. He had a great love for that country and its people, and intended to return there to make his home. He was educated at Sakeji School, Northern Rhodesia, then at Monkton Combe, in Somerset. He studied medicine at King's College, London, and Westminster Hospital, where his father and an uncle had been students and where two of his sisters were nurses. He was popular with his fellow students and teachers and took part in many hospital activities. In particular, his fitness and determination played a great part in the improving fortunes of the Rugby club, of which he was vice-captain in 1947–8. He studied seriously, gaining in 1949 the Hanbury prize and the Frederick Bird medal and prize. Having graduated M.B., B.S. of London University in 1949, he was appointed house-surgeon first at Westminster Hospital and then at the Royal Northern Hospital. There followed his period of National Service in the Royal Air Force, when he was stationed in Southern Rhodesia. During this time he made several trips into the jungle, and his enthusiastic description of these was full of wonder and delight. After his return to England he was house-surgeon at the Hospital for Sick Children, and in 1954 was admitted F.R.C.S. He became registrar to Sir Clement Price Thomas at Westminster, where he decided upon thoracic surgery as a career and then spent a year as resident surgical officer at the Brompton Hospital. At the time of the expedition he was on leave from the Rathbone Hospital, Liverpool, where he was thoracic surgical registrar.

Though we had been students together since King's College days in 1944 and housemen together at Westminster, it was during this latter period at the Brompton that I really came to know Chris well. Many hours were spent in his company talking of thoracic surgery, of mountaineering, of future travels, or listening to classical music. It is difficult to say which of these was his greatest love. All his activities were pursued to the utmost of his ability, and it was typical that he enjoyed every moment of everything he did. Having, one Christmas, agreed to write and act in a residents' show for the patients, he tackled this with his customary zeal and was instrumental in making it a great success, in spite of the pressure of his surgical duties at that time. He made friends spontaneously even when there was the barrier of language. Possessing a sense of humour, he passionately believed that whatever course of action he took was right, and spared no effort in his care of his patients. He had great courage and integrity, the result of his home life and religious upbringing, and had much to give to life and many friends. He was only 32, and not yet married. If he had to die, he would not have wished to change the manner of his dying, for he loved the challenge of high places. His family and friends have suffered a grievous loss in this tragic accident. I am proud that I was his friend.

Dr. W. M. EDGAR writes: Chris Hoyte was a keen mountaineer and spent much of his spare time climbing in North Wales. On the many occasions we climbed together, both in Wales and abroad in the Alps and Corsica, he was an ideal companion in whom one had complete trust. At the end of long and tiring climbs he still had energy left, and did not lose his sense of humour even at the most trying moments. He was ambitious and always ready to attempt difficult climbs, but, although not easily admitting defeat, he knew when to do so. As with all who become mountaineers, mountains were to him an irresistible lure, but he had many other interests and was always stimulating to be with. His early death is tragic, and he is sadly missed by all his friends.

Drs. A. E. MOURANT and H. LEHMANN write: It was solely a love of mountaineering which led Christopher Hoyte to join the expedition which was to attempt the first ascent of Minapin peak in the Karakoram mountains. But at the same time he offered to carry out medical investigations on the populations of the region, and in consultation with the Medical Research Council it was decided that he would collect specimens for the examination of abnormal haemoglobins in Sind, and also from the isolated Hunza tribe, for detailed blood grouping, haemoglobin examination, and immunological testing. At his untimely death he had already carried out the first part of this programme, and the specimens he collected from Sind have supplied an important anthropological link between South India, Arabia, and Africa in the form of the first example of the sickle-cell trait from West Pakistan. It is with gratitude that we are able to say that Mr. Dennis Kemp, one of the survivors of the expedition, has offered, with the help of Major Rahmen, the Gilgit Agency doctor, to complete the investigations which Christopher Hoyte had undertaken.

H. E. DYSON, M.D.

Dr. H. E. Dyson, who was in general practice at Wembley for 40 years, died at his home at Hosey Hill, Westerham, Kent, on June 28. He was 76 years of age.

Harold Edward Dyson was born at Halifax on September 7, 1881. A Salters exhibition from the City of London School took him to University College and Hospital, where his further awards included the Atkinson Morley Scholarship. He obtained the London Conjoint diploma in 1904, and in the following year the London degrees of M.B., B.S. He held house appointments under Professor Bilton Pollard, Professor Percy Flemming, and Sir John Rose Bradford at University College Hospital, and, after obtaining his M.D. in 1907, settled in general practice at Wembley, where he remained until 1946. He leaves a widow, one daughter, and one son.

H. M. H. writes: The generation of practitioners qualified before 1914 has lost a worthy representative in the death of Dr. H. E. Dyson. It was at Wembley that he did his life work, as partner to the late Dr. Charles E. Goddard and his son Dr. C. Ambrose Goddard. The association was more than a professional one, for in 1918 Dyson married his senior partner's daughter, and for a generation the combined families were prominent in the developing life of the district. The youngest son of the Rev. Watson Dyson and brother to Sir Frank Dyson, sometime Astronomer Royal, Dr. H. E. Dyson was well fitted by tradition and temperament for his work. When plans to found a voluntary hospital at Wembley came to fruition in 1928, he and his wife were among the first to serve on its committees. Through the years, until his retirement in 1946, his colleagues looked to him for balanced, sane, and courageous advice, for he brought a wide culture to bear on all problems. He never forgot his classics and had an ear for the felicitous phrase. In 1928–9 he was chairman of the Harrow and Uxbridge Division of the B.M.A. From 1916 to 1918 he served in France, and in the second world war in the Home Guard. A lifelong lover of games, he excelled at golf. It is not, however, for his activities that we best remember him. It is his personality that remains—his utter integrity, his cheery greeting, and ready smile. Of Yorkshire descent, he did

not wear his heart on his sleeve, and his light-hearted manner hid a deep human understanding. Had he been willing to reveal himself so far, he might often have quoted: "If I did not laugh, I should cry." The last time I saw him, when he had already suffered a severe illness, he reminded me of a conversation of many years ago concerning Osler's essay "Aequanimitas." "I still try," he said, "to live it." It was the most revealing thing I ever heard him say.

E. A. SMITH, Ch.M., M.B., F.R.C.S.

Mr. E. A. Smith, who practised as a general practitioner and as a surgeon in Vancouver after a distinguished early career in England, died at his home at Wells, Somerset, on June 25, aged 83.

Edward Archibald Smith was born near Rotherham on March 12, 1875. He was educated at Wesley College, Sheffield, the Yorkshire College, Leeds, and University College, Liverpool, where he studied medicine. Graduating M.B., Ch.B., with first-class honours, from the Victoria University, Manchester, in 1896, he held the appointments of house-surgeon and medical registrar and tutor at the Liverpool Royal Infirmary. He was admitted F.R.C.S. in 1900 and obtained the degrees of M.B. at the University of Liverpool in 1904 and Ch.M. at Manchester in 1909. After a period in general practice at Southport he spent two years, from 1906 to 1908, in postgraduate study on the Continent, visiting the university teaching centres at Berlin, Heidelberg, Vienna, and Paris. He then set up in consultant surgical practice in London, being elected honorary surgeon to the Western General Dispensary. In 1908 he published a monograph entitled *Suture of Arteries*, and a year or two later he received a B.M.A. scientific grant to continue his research on vascular surgery. One of his papers on the subject was published in this *Journal*. He went out to British Columbia in 1911 and practised in Vancouver, where he was honorary surgeon at St. Paul's Hospital. He retired to live first at Jersey and later at Wells.

J. H. M. writes from Vancouver: *Eheu! fugaces . . . labuntur anni.* It is 29 years since Dr. Archibald Smith withdrew his name from the *Register* of the College of Physicians and Surgeons of British Columbia, when he left the province to go to England; and few of us remain to remember him or record his doings here, though he was a most active and energetic practitioner of medicine here for some eighteen years. There are few notes available about him: we know that he had English degrees in medicine and was very well qualified. So most of what we have to say about him is based on personal memories. He was a big, bluff man, always on the go, and bubbling over with energy. He would frequently see the same patient, or several of them, two or three times a day, at home or in the hospital, or oftener if he thought it necessary. One's visual memory of him might be called, after the manner of the old Dutch school of painting, "Portrait of a Man and a Pipe," for one never saw him without a pipe in his mouth, firmly clamped there. He never took it out, apparently; he talked round it, gave orders to nurses round it, and wrote orders or reports through its reek, and in fact lived with it. Presumably he took it out to eat, or when he went to bed, but we have no record of this; tobacco seems to have done him nothing but good, as he lived to a ripe old age. Personally he was a friendly, pleasant man to meet, keenly devoted to his work, and always ready to discuss a case. The writer of this knew him only as a fellow doctor whom one met often in the wards, and knew little or nothing of his family life or his private tastes and avocations—but one remembers that he did a good deal of surgery, and did it well. As was the custom in Vancouver in those days, he was a general practitioner who did surgery as it came to him in his practice—he did not confine his work to surgery entirely. His abundant energy and vitality carried him through a tremendous day's work. He was well liked by his colleagues.

Medical Notes in Parliament

QUESTIONS IN THE COMMONS

Tuberculosis Beds

The Rev. R. W. SORENSEN (Leyton, Lab.) asked the Minister of Health on July 21 to what extent hospitals for the treatment of tuberculosis had been closed down or reduced during the past five years; and how many beds were now reserved for patients suffering from some form of this disease compared with 1953. Mr. D. WALKER-SMITH said the number of hospital beds allocated to tuberculosis in England and Wales decreased by 8,935 between December 31, 1952, and December 31, 1957, when the numbers were 35,293 and 26,358 respectively.

Mr. SORENSEN asked to what general cause or causes the Minister attributed this encouraging decline. Could they take it that some of the hospitals previously used for the treatment of tuberculosis were now being used as general hospitals? Mr. WALKER-SMITH said he thought the root cause of the decline was the advances in medicine and science in dealing with this matter, which was very gratifying indeed. As to surplus accommodation, the hospital authorities were, of course, well aware of the importance of ensuring that beds no longer required for the treatment of tuberculosis were, when suitable, put to some other use, but inevitably there was some time lag on occasion in effecting the appropriate switch-over. Dr. EDITH SUMMERSKILL (Warrington, Lab.) asked what his policy was in allocating these beds to patients suffering from other diseases? Mr. WALKER-SMITH said his policy was to make the best use at the earliest possible moment of all accommodation that became available.

Consultants' Merit Awards

The MINISTER OF HEALTH was asked by Mr. ELLIS SMITH (Stoke-on-Trent, South, Lab.) for the amounts paid in each year since the inception of the Health Service in merit payments, and for a statement on the administration of the scheme, indicating the basis on which merit payments were made and giving examples of the individual amounts paid. He made the following statement in reply:

"Awards are made on the recommendations of a Committee set up to advise my right hon. Friend the Secretary of State for Scotland and myself which consultants should receive awards for professional distinction. Four per cent. of consultants receive awards at the rate of £2,500 a year for whole-time employment, 10% at the rate of £1,500, and 20% at the rate of £500. Part-time consultants receive a fraction related to the amount of time for which they are employed in the hospital service. The number of awards in payment in England and Wales at the end of 1957 was: 376 at £2,500, 690 at £1,500, and 1,377 at £500.

"Information about the actual amounts paid is not readily available, but it is estimated that the amounts would be approximately:

	£
1948 (6 months)	680,000
1949	1,450,000
1950	1,550,000
1951	1,650,000
1952	1,740,000
1953	1,820,000
1954	1,850,000
1955	1,890,000
1956	1,920,000
1957	1,960,000

"The basic salary of consultants holding awards at the rate of £2,500 or £1,500 is abated by £300 and £200 respectively (or in due proportion in the case of part-time appointments)."

Doctors' and Dentists' Pay

Mr. A. M. F. PALMER (Lab.) asked the Chancellor of the Exchequer what approach had been made to the Trades Union Congress, the National Federation of Professional Workers, individual trade unions, and the statutory salary-negotiating bodies in the nationalized industries by the Central Office of Information in connexion with the inquiries it was making for the Royal Commission on Doctors' and Dentists' Remuneration. Mr. J. E. S. SIMON, Financial Secretary to the Treasury: None.

Medico-Legal

INFECTED BLOOD TRANSFUSION

[FROM A HAEMATOLOGIST]

On April 16 a man of 52 was admitted to Mayday Hospital, Croydon, suffering from recurrent haematemesis and melaena, and on the 17th it was decided that he should receive a blood transfusion. Three bottles were cross-matched, but about 20 or 30 minutes after the second bottle was started the patient became distressed and his legs started to twitch; 50 mg. promethazine hydrochloride was administered and he slept for an hour, awakening with severe back pain and a shivering attack. The transfusion was stopped, but three hours later, at 8 p.m., his pulse was imperceptible and his blood pressure 90/60, so a further transfusion of three bottles was given during the next eleven hours, at the end of which his blood pressure had fallen further, to 80/50, and fresh blood was present in his stools. Transfusion was continued without response. About 1 p.m. on the 18th the registrar saw him for the first time that day, noted the blotchy erythema and icteric tinge, and found that he had passed no urine for 24 hours; he decided that the most likely cause of this curious condition was something to do with the transfusion, set up a noradrenaline drip, and called in the pathologist, but the patient's condition steadily deteriorated and he died early the next morning. At necropsy the pathologist found changes indicating acute septicaemia, compatible with the transfusion of infected blood. The bottle suspected of causing the trouble had been left at room temperature from 6 p.m. on the 17th to 2 p.m. on the 18th before it was cultured and found to be contaminated; by the 19th, when it was returned to the Regional Blood Transfusion Depot, it stank.

No information on the contaminating organism or its numbers is available to the writer.

The bottle which caused this tragedy seems to have had an eventful history. Collected at Worthing on March 25, it was sent to Mayday Hospital the next day, and while there was entered to obtain blood for cross-matching no fewer than seven times. Further, it reached the usual expiry date of 21 days on April 15, and should have been returned to the depot on that day; but the technician performing the cross-match altered the expiry date to April 20 without consulting anyone, explaining that if he had not altered the date there would have been a shortage. The director of the South London Blood Transfusion Centre stated in evidence, however, that there was no shortage of blood of the patient's group between April 16 and 18. He also stated that there was no recognized limit to the number of times a bottle might be entered to obtain blood for cross-matching; it was entirely at the discretion of the laboratory using it. He had never known an organism enter a bottle when a correct sterile procedure was carried out.

At the subsequent coroner's inquest (*Croydon Advertiser*, May 23) a verdict of death by misadventure was returned.

Comment

The circumstances of this tragedy raise a number of problems which have not yet been solved. First is the possibility of entering a blood bottle without contaminating its contents. The director of the blood transfusion centre expressed the opinion that this was possible if standard bacteriological technique is adopted, but others are less certain; in the United States the bottle must not be entered before transfusion,[1] and the 1954 edition of *Notes on Transfusion* issued by the Ministry of Health stated that if a bottle of blood was entered it must be labelled "Dangerous for Patients" after the lapse of 24 hours. This dictum gave rise to a storm of criticism and has been omitted from the most recent edition (1958) of the pamphlet. McEntegart[2] expressed the opinion that, if properly refrigerated, blood, even when contaminated with cryophilic organisms, rarely becomes dangerous until the third week of storage; but James and Stokes[3] are less sanguine, and in their experimental studies obtained heavy growth after six days. It would seem safest to assume that the bottle is contaminated every time that it is entered, and that after about 72 hours any cryophilic bacteria introduced will have multiplied enough to endanger the recipient.

Second is the problem of how to eliminate these dangerous cryophilic bacteria which cause most of the deaths.[3,4] This is not easy. They have been found in the liquid in which viscose caps are stored and on cotton-wool in the laboratory; they are resistant to many antiseptics. If alcohol is applied to the rubber seal with a swab, unless the swab has been sterilized and maintained sterile, it may easily contaminate the surface it was meant to sterilize. This would seem an added argument against multiple puncture.

Some blood transfusion centres are averse to using pilot bottles or find that pathologists in their areas distrust them. Experience elsewhere, particularly in Sheffield and in North London, suggests that such misgivings are unjustified. Even if the pilot bottle were used but once it would afford appreciable protection, for the number of bottles which need to be cross-matched more than twice must be very small. Few laboratories have a satisfactory system of indicating whether a bottle has previously been entered or cross-matched. Some laboratories indicate this by transferring an adhesive label from the side of the bottle to the cap, but this is not ideal. Some pathologists still examine each bottle for bacteria before issuing it; but these are in a very small minority, and seem to be concentrated in those areas where pilot bottles are not used. It might, after all, be simpler and safer for them to adopt pilot bottles, since James,[5] who uses them in North London, has had only one contaminated bottle among 900,000 issued. I know of no serious accident due to the use of Campbell's[6] holder or its modifications.

It is difficult to understand the point of altering the date of expiry on a label. It is quite permissible, of course, for a pathologist to tell a clinician that the blood offered is more than 21 days old, but that in the circumstances prevailing it is the best available and should at least do no harm (for many years the expiry time for blood was 28 days after collection, and Prankerd[7] has administered blood 42 days old); but to alter a label is another matter.

Finally, there is the question of how the laboratory services are organized. A considerable number of these blood transfusion accidents seem to have occurred in hospitals which are served by laboratories staffed and organized by a central group laboratory, from which junior pathologists are sent out to do duty at the smaller laboratories. Such laboratories have done yeoman service in helping to upgrade many of the former workhouse infirmaries into sound general hospitals; but, although they allow maximum technical skill to be applied to every problem which reaches them, it is not always certain that every important problem does in fact reach them, or that their technical skills can be fully applied to patients in other hospitals within the group. Further, if technicians remain permanently in a subsidiary laboratory, supervised by a registrar whose purely technical knowledge may be less than their own, and only occasionally visited by a consultant, those technicians may easily develop their own private techniques which give results different from those obtained by standard procedures—and the consultant may remain in ignorance of very important changes. The logical conclusion is that every good-sized general hospital should have a full-time or nearly full-time clinical pathologist of consultant status to take special care of blood transfusion and hygiene, and that he should have at his command the resources of reference laboratories which could serve several groups.

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£12,000 DAMAGES FOR DOCTOR'S DEATH IN ATTEMPTING RESCUE

[FROM OUR LEGAL CORRESPONDENT]

On August 17, 1955, Dr. Mark Gregory Baker, of Ashby-de-la-Zouche, was stopped by the police on his rounds and called to a 50-foot (15-m.) well at Tadser Farm, Ticknell, in which two men had been overcome by fumes. They were inspecting the well, and a petrol-driven pump had been installed to empty the water, which was some 12 ft. (3.5 m.) deep, on a platform 28 ft. (8.5 m.) below ground level. The motor had been run for about an hour on the evening before.

On arrival Dr. Baker tied two pieces of rope together with a loop round his waist, and told the farmer's daughter and another woman who was with her to pull him up if he called out. He then went down, and after a bit called out that he thought there was nothing he could do for the men, and said he would come up in a minute. The farmer's daughter later asked if he was all right, and when he answered "No" they tried to pull him up on the rope but could not because it fouled an obstruction. When the fire brigade arrived a fireman with breathing apparatus brought Dr. Baker to the surface still alive, but he died from carbon-monoxide poisoning on the way to hospital. The other two men were dead when brought up.

Dr. Baker's widow, who before the accident had practised in partnership with him, brought an action on behalf of herself and their two children against the employers of the two men whom he had tried to rescue. Her case, heard in the High Court this month (*The Times*, July 15, 17, 18, and 22), was that the employers were negligent in that it was highly dangerous to let their men go down a well in which a petrol-driven pump had been used with no safety apparatus and no means of testing the air, and that they had given no adequate warning to their employees of the danger. Moreover they owed a duty of care not only to their employees but to Dr. Baker, because it was the reaction of human nature to save life if a call came for help, and a person whose negligence was responsible for the call for help was liable in damages to anyone who was injured in answering the call.

Brave and Humane

On July 21 Mr. Justice Barry gave judgment for Mrs. Baker for £12,000. He said that the reasonableness of Dr. Baker's conduct had been challenged and it had been alleged by way of defence that he had voluntarily undertaken the risk. It was beyond doubt that Dr. Baker had acted from an urgent and passionate desire to do everything he could, even at a great risk to himself, to preserve human life. It would be a slight on his profession to hold that such conduct on the part of a brave and humane doctor could not reasonably be contemplated by those whose negligence created the peril which he sought to arrest.

The judge directed that of the damages £2,000 should be paid to trustees on behalf of each child to administer for them until they were 21. He granted a stay of execution pending appeal.

Vital Statistics

England and Wales in 1957

Cancer of the lung and influenza were the main causes of death to show an increase in 1957 over the figures for the previous years. Deaths from lung cancer numbered 19,120, compared with 18,186 in 1956. Deaths from influenza numbered 6,715, compared with 2,626 in 1956 and 2,983 in 1955. On the other hand, deaths attributed to bronchitis decreased by 2,740, from 29,670 to 26,930. A rise of 80 over the 1956 total was recorded for deaths due to leukaemia, from 2,315 to 2,395. There were 88 deaths from whooping-cough, 95 from measles, 10 from enteric fever, 184 from meningococcal infections, 10 from scarlet fever, 4 from malaria, and 2 from smallpox. Deaths from respiratory tuberculosis numbered 4,249 and were 604 fewer than in the previous year.

First Quarter of 1957.—The effects of last year's Asian influenza epidemic were shown in the first quarter of this year by increased mortality from pneumonia and influenza. Death rates per million population, with the figures for the first quarter of 1956 in parentheses, were: pneumonia 1,042 (574), influenza 178 (32). Other statistics for the first quarter appeared in the *Journal* of May 3, page 1074.

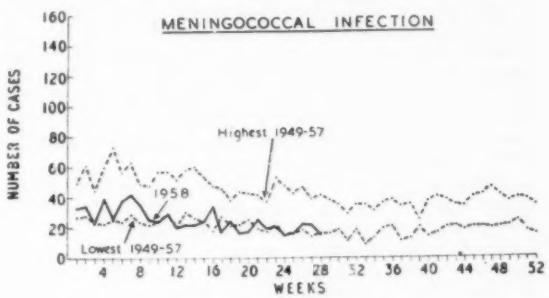
Second Quarter of 1957.—The infant mortality rate reached a record low figure for the second quarter of 21.3 per thousand live births. This was 1.0 below last year's figure for the second quarter, the previous lowest. The birth rate of 16.9 per thousand population was the highest for a second quarter since 1949, when the rate was 17.6; last year's comparable rate was 16.6. The general death rate was 11.1 per thousand population, which was 0.5 above the rate for the second quarter last year. The stillbirth rate reached the low figure of 21.4 per thousand live and stillbirths, which was 1.7 below the rate last year.

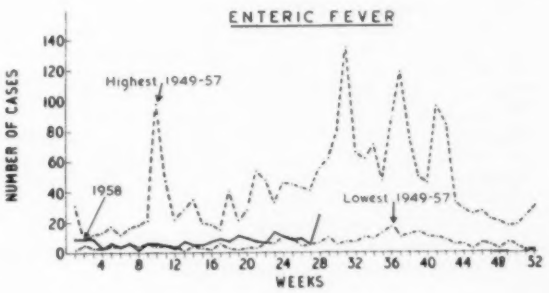
Venereal Diseases

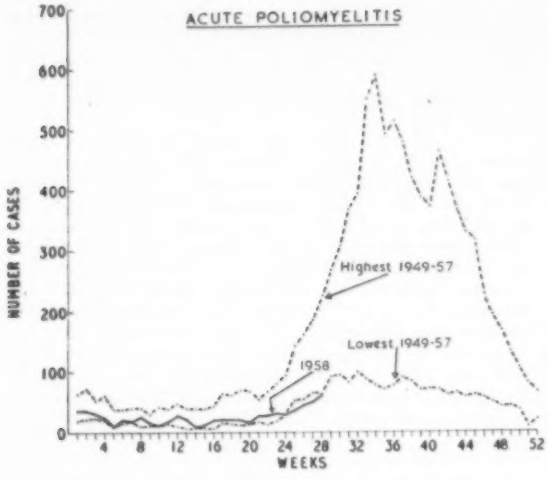
In England and Wales during the quarter ending December 31, 1957, 1,144 new cases of syphilis were reported as attending the clinics, as compared with 1,291 the previous year. Of these, 175 were classified as primary, secondary, or latent in the first year of infection. 10 cases of congenital syphilis in children aged under 1 year were reported, and 122 cases in persons over that age. New cases of gonorrhoea (with corresponding 1956 figures in parentheses) numbered 6,244 (5,416), of chancroid 57 (80), and of non-gonococcal urethritis (males only) 3,717 (3,678).—*Monthly Bulletin of the Ministry of Health*, June, 1958.

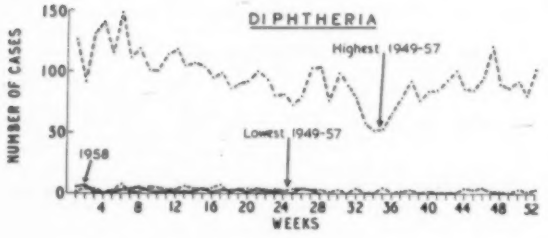
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1949–57 are shown thus ------, the figures for 1958 thus ————. Except for the curves showing notifications in 1958, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending July 19

The largest variations in the trends of the notifications of infectious diseases were a decrease of 404 for measles, from 7,078 to 6,674, and 28 for dysentery, from 740 and 712, and increases of 105 for food-poisoning, from 227 to 332, 26 for scarlet fever, from 625 to 651, and 11 for whooping-cough, from 816 to 827.

The largest falls in the incidence of measles were 152 in Derbyshire, from 287 to 135, and 127 in Nottinghamshire, from 376 to 249; the largest rises were 77 in Warwickshire, from 230 to 307 (Birmingham C.B. 229), and 64 in Gloucestershire, from 169 to 233 (Bristol C.B. 122). The largest increases in the number of notifications of whooping-cough were 27 in Hampshire, from 31 to 58, 23 in Durham, from 48 to 71, and 23 in Warwickshire, from 39 to 62; the largest decreases were 50 in Sussex, from 71 to 21, and 28 in Gloucestershire, from 64 to 36. No large fluctuations in the returns of scarlet fever were recorded. 3 cases of diphtheria were notified, compared with none in the preceding week.

The notifications of acute poliomyelitis numbered 57, and these were 2 more for paralytic and 4 fewer for non-paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding 17 (Bradford C.B. 5, Leeds C.B. 5, Todmorden M.B. 2, Rotherham R.D. 2), Essex 6 (Southend-on-Sea C.B. 2), Lancashire 5 (Manchester C.B. 2), and Yorkshire East Riding 5 (Haltemprice U.D. 5).

The chief centres of dysentery were Yorkshire West Riding 137 (Barnsley C.B. 28, Thorne R.D. 25, Bradford C.B. 12, Huddersfield C.B. 12, Sheffield C.B. 11, Leeds C.B. 10), Lancashire 112 (Manchester C.B. 27, Liverpool C.B. 15, Widnes M.B. 14), London 105 (Islington 21, Bermondsey 16, Hackney 15, Deptford 13, Wandsworth 11), Nottinghamshire 41 (Nottingham C.B. 37), Durham 36, Warwickshire 30 (Birmingham C.B. 14, Coventry C.B. 10), Essex 27 (Walthamstow M.B. 14), Surrey 23 (Kingston-upon-Thames M.B. 11), Staffordshire 21, and Cheshire 21.

The largest outbreak of food-poisoning during the week was 59 notifications in Manchester C.B.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **July 12** (No. 28) and corresponding week 1957.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1958					1957				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	1	0	1	3	0	0	0	1
Dysentery ..	740	91	158	14	2	465	23	123	9	3
Encephalitis, acute	4	2		1		2	0	0	0	
Enteric fever:										
Typhoid ..	18	0	0	0		2	1	0	1	
Paratyphoid ..	4	1	2(B)	0		4	0	0	0	
Food-poisoning ..	227	33	27	1		418	41	46	0	
Infective enteritis or diarrhoea under 2 years				20	25				11	26
Measles *	7,078	537	62	50	21	13,417	344	128	97	185
Meningococcal infection	15	2	9	0		16	2	11	3	
Ophthalmia neonatorum	12	1	3	0		20	0	5	0	
Pneumonia† ..	220	21	134	2		197	8	106	2	
Poliomyelitis, acute:										
Paralytic ..	35	2	20	2	14	68	8	3	10	3
Non-paralytic ..	24	2				65	6			
Puerperal fever§ ..	229	30	13	2		215	36	1	2	1
Scarlet fever ..	625	55	57	11	20	413	37	46	17	25
Tuberculosis:										
Respiratory ..	497	72	64	11		550	67	126	11	
Non-respiratory	70	4	11	2		97	6	13	4	
Whooping-cough ..	816	39	53	21	44	1,661	69	76	4	35

DEATHS	1958					1957				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	No comparable figures available.	0	0	0	0
Dysentery ..	1	0		0			0	0	0	
Encephalitis, acute		0			0		0			0
Enteric fever ..	0	0	0	0			0	0	0	
Infective enteritis or diarrhoea under 2 years	5	0	0	0	0		0	3	1	0
Influenza	8	0	0	0	1		0	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia ..	301	29	15	12	1		14	10	5	8
Poliomyelitis, acute	4	0		0	0		0		1	0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	57	1	3	0	2		7	7	0	3
Non-respiratory		3	2	1	1		0	1	0	1
Whooping-cough ..	0	0	0	0	0		0	0	0	0
Deaths 0–1 year ..	284	26	38	5	17		21	20	4	12
Deaths (excluding stillbirths) ..	8,274	693	514	94	165		605	434	68	160
LIVE BIRTHS ..	13,676	1127	888	185	421		1174	926	217	450
STILLBIRTHS ..	287	22	22				23	18		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

President, Welsh National School of Medicine.—The court of the University of Wales has elected Sir CLEMENT PRICE THOMAS president of the Welsh National School of Medicine. This office is that of head and chief officer of the school and is tenable for five years in the first instance. Sir Clement, who is surgeon to the Westminster and Brompton Hospitals, is an old student of the school.

Royal College of Obstetricians and Gynaecologists.—Two new vice-presidents of the College were elected at the meeting of the College council on July 26—Mr. G. F. GIBBERD, of Guy's, and Mr. S. W. MASLEN-JONES, of Wolverhampton. The other officers were re-elected and are as follows: *President*, Professor A. M. CLAYE; *hon. treasurer*, Mr. A. C. H. BELL; *hon. secretary*, Mr. I. M. JACKSON; *hon. librarian*, Mr. A. J. MCNAIR; *hon. curator of the museum*, Mr. R. A. BREWS; *hon. treasurer, Australian Regional Council*, Mr. J. N. CHESTERMAN; *hon. treasurer, Canadian Regional Council*, Dr. G. A. SIMPSON; *hon. treasurer, New Zealand Regional Council*, Dr. A. M. RUTHERFORD; and *hon. treasurer, South African Regional Council*, Dr. F. N. CHARNOCK.

Paediatric Surgeons.—The feature of the annual dinner of the British Association of Paediatric Surgeons was the presence of a large number of paediatricians from other countries: from Australia, Austria, Czechoslovakia, Denmark, Egypt, Finland, Germany, Greece, Holland, Italy, Japan, Malta, Poland, Sweden, Switzerland, U.S.A., and Yugoslavia. Miss ISABELLA FORSHALL, this year's president, said in her speech of welcome that Mr. A. W. WILKINSON had this year been appointed to the first chair of paediatric surgery in Britain. Mr. DENIS BROWNE was the first non-American to receive the William E. Ladd medal for work in paediatric surgery. Miss Forshall gave a special word of welcome to the doyen of British paediatric surgeons, Mr. TWISTINGTON HIGGINS, to Sir JAMES PATERSON ROSS, P.R.C.S., to Sir JOHN CHARLES, and to the Moynihan and Simpson-Smith lecturer, Dr. WILLIS POTTS, of Chicago, an honorary member of the B.A.P.S. Replying for the guests Dr. POTTS said he was fascinated by the speed of development of paediatric surgery in Britain, far more rapid than in the U.S.A.

Sensationalism in Medicine.—Speaking about the Hospital Service's special place in the public's regard, in the course of an address to the Scottish Western Regional Hospital Board on the first decade of the N.H.S., Dr. A. K. BOWMAN, the board's senior administrative medical officer, said: "One must hope that the almost morbid interest which it has engendered will not of itself become a new epidemic disease, for the effective work of medicine cannot be carried on in an atmosphere of sensationalism." Amplifying his remarks later to a reporter (*Scotsman*, July 23) Dr. Bowman said he feared an increase in hypochondriac tendencies, and even the development of neuroses, among people absorbing the wide range of television programmes and press articles on medicine. Already it had been noted that people were going to their doctors with vague fears and anxieties about their health. The impact on their minds of watching a television programme on a new treatment could convince them that they might have the symptoms of the disease. A programme from the Western Infirmary, Glasgow, on the use of radioactive iodine in endocrine disorders had sent several people to their doctor, self-convinced they were ill. Dr. Bowman had heard of only one case in which a programme such as this had had a fortunate result.

Fluoridation at Andover.—Last month the Andover Borough Council decided to stop fluoridation of the town's water supply. This decision was taken after considerable pressure from the town's inhabitants and after the election in May of a number of councillors pledged to oppose fluoridation. Last year a similar motion was defeated by one vote, and in January this year the local anti-fluoride association sought to prevent the council from continuing its fluoridation programme by a relator action in the courts (see *Journal*, February 8, p. 348). Andover was one of the four areas in Britain chosen by the Ministry of Health some three years ago to demonstrate the effects of fluoridated water. The other areas were Anglesey, Kilmarnock, and Watford.

I.T.V. and Smoking.—The Independent Television Authority has banned advertisements for cigarettes or tobacco during programmes for children. The I.T.V. companies have also been advised not to show such advertisements either just before or just after the programmes.

Carlsberg–Wellcome Fellowships.—The Carlsberg Foundation (Copenhagen) and the Wellcome Trust (London) announce a second series of awards of the Carlsberg–Wellcome travelling research fellowships. The successful candidates for 1958–9 are Dr. S. E. JENSEN and Dr. D. A. T. DICK. Dr. Jensen (Aarhus University) will work at the Postgraduate Medical School of London, and Dr. Dick (Oxford University) will work at the Carlsberg Laboratory.

M.R.C.O.G.—The following candidates have been elected to the membership of the Royal College of Obstetricians and Gynaecologists:

P. Aiman, P. H. Amarasinghe, D. T. C. Barber, C. T. H. Barrett, W. P. Bonnici, J. Breeze, J. M. Brudenell, D. P.-C. Chan, H. J. H. Claassens, C. J. T. Craig, D. R. Das, R. M. Davie, R. F. Drake, G. R. Duncan, G. H. Ellidge, W. H. Fernando, L. H. Fienberg, J. M. G. Harley, D. Heginbotham, J. M. Hemsley, A. H.-L. Hsu, P. J. Huntingford, S. R. Ingold, K. I. Jack, R. D. Johnstone, E. W. P. Jones, A. J. Keane, A. C. Keast, D. M. D. King, S. V. Kinley, D. R. Lowe, J. McGlone, S. Malhotra, G. S. Mandal, D. T. Mathews, C. C. Mitra, D. Montgomery, W. P. L. Morrison, A. D. Muirhead, S. Muscat, S. H. P. Nanayakkara, I. R. Napier, H. J. Pash, J. H. Peters, D. W. Pfanner, C. M. Rant, D. M. Reader, W. J. C. Rebello, J. St. George, A. K. Sarkar, P. C. Stichbury, J. O. Struthers, W. M. E. Tweed, R. N. Udipi, T. Visvanathan, A. W. G. Weir, D. J. Whitney, W. G. Wicks, and B. Yoganathan.

M.R.C.P.Ed.—At a quarterly meeting of the Royal College of Physicians of Edinburgh on July 22 the following were elected members:

T. E. Anderson, T. N. Macgregor, W. Sircus, P. M. Yap, M. F. H. Kelleher, K. K. Gupta, A. S. Jureidini, R. V. K. Alwa, M. A. Ghani, M. M. Hassan, J. M. Hughes, K. J. Cullen, E. A. Kauffmann, J. Chatterjee, L. B. T. Jayasundera, J. G. Wijeyesekera, R. P. Sharma, N. H. Gopaldas, J. D. E. Knox, A. P. J. Weerasekera, R. K. Parida, J. Schneider, B. W. Petty, A. A. Akiwumi, E. Hanam, D. A. Seaton, R. D. Catterall, J. H. A. Dwek, R. N. Gupta, D. Zentkowsky, H. C. Kwaan, M. H. Myint, T. S. Koshy, A. A. Hameedi, D. Narula, R. J. Buhariwalla, C. T. Lee, W. H. Schutt, H. Stark, B. G. Gandhi, Y. K. Lee, K. P. Jain.

Leprosy Research Fund.—Five years ago, at the instigation of Dr. R. G. COCHRANE, who had been appointed its technical medical adviser, the American Leprosy Missions, Inc., set up a Fund, with a laboratory in London, with the stated object of correlating work on leprosy more closely with medical research generally. This Fund, with limited resources, assists pilot research projects and inquiries and undertakes preliminary clinical trials. It also hopes to organize a leprosy reference laboratory and histopathological registry. Further details are obtainable from Dr. Cochrane, 11a, Weymouth Street, London, W.1.

Gerontological Abstracts.—*Excerpta Medica* has added another to its series of medical abstracting journals. This is *Gerontology and Geriatrics*, published in co-operation with the U.S. National Health Institute and the U.S. National Institute of Mental Health and aided by a grant from the U.S. Public Health Service. *Gerontology and Geriatrics* will appear monthly, at an annual subscription of £5 13s., from the Excerpta Medica Foundation, 111, Kalverstraat, Amsterdam.

Edinburgh University.—After the graduation ceremonial on July 16 the Cameron prize in practical therapeutics was awarded to Dr. C. B. HUGGINS, professor of surgery at Chicago University, in recognition of his researches on the hormonal treatment of cancer "and particularly for his introduction of the treatment of prostatic carcinoma by oestrogens."

St. Andrews University.—Dr. D. M. GREEN has been promoted to become senior lecturer in the department of bacteriology at Queen's College. He was appointed lecturer there in 1949.

"Family Doctor."—In the August issue Dr. RICHARD ASHER tells the reader "The Truth about Harley Street." Other articles deal with bites and stings, allergy, and the cult of the bathroom. There are also regular features such as "Family Doctor Answers" and "Under Five Forum."

Professor John Craig, of the department of child health at Aberdeen University, has been made an honorary fellow of the American Academy of Pediatrics.

COMING EVENTS

Ars Medica Exhibition.—Until August 8 at the Welsh National School of Medicine, Cardiff; August 18–22 at Bristol University; August 25–29 at the West Middlesex Hospital, Isleworth.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Industrial Medicine.—Issued quarterly (£3 annually). The new issue Vol. 15, No. 3, includes :

THE ACCURACY OF OCCUPATIONAL VITAL STATISTICS. M. A. Heasman, F. D. K. Liddell, and D. D. Reid.
THE INFLUENCE OF CLOTHING ON THE PATTERN AND SEVERITY OF BURNS STUDIED IN SOME RECENT COLLIERY FIRE-DAMP IGNITIONS. M. N. Tempest and J. B. Atkins.
THE TOXIC PROPERTIES OF DEMETON-METHYL ("METASYSTOX") AND SOME RELATED COMPOUNDS. M. Vandekar.
TISSUE REACTIONS PRODUCED BY CALCIUM FLUORIDE IN THE LUNGS OF RATS. E. J. King, M. Yoganathan, and G. Nagelschmidt.
THE TISSUE REACTION IN THE LUNGS OF RATS AFTER THE INHALATION OF COAL DUST CONTAINING 2% OF QUARTZ. E. J. King, S. Zaidi, C. V. Harrison, and G. Nagelschmidt.
PNEUMOCONIOSIS OF COAL-MINERS IN THREE NORTHUMBRIAN COLLIERIES. R. I. McCallum and D. J. Newell.
INDUSTRIAL DERMATITIS IN THE COAL-MINER. O. P. Edmonds.
LESIONS OF THE SKIN IN PROCESS WORKERS CAUSED BY CONTACT WITH BUTYL TIN COMPOUNDS. W. H. Lyle.
CLIMATE AND HEALTH IN THE ROYAL NAVY. F. E. Smith.
THE EMOTIONAL STABILITY OF MINERS WITH NYSTAGMUS. Judith S. Lion.
A CASE ILLUSTRATING THE EFFECT OF CALCIUM DISODIUM VERSENATE ($CaNa_2E.D.T.A.$) ON CHRONIC MERCURY POISONING. S. M. Woodcock.
A CASE OF BERYLLIUM DISEASE. C. H. Wood, K. P. Ball, and N. Donald Teare.

Journal of Clinical Pathology.—Issued six times a year (£4 4s. annually). The new issue, Vol. 11, No. 4, includes :

A RE-ASSESSMENT OF THE GASTRIC LESION IN PERNICIOUS ANAEMIA. H. A. Magnus.
RENAL PAPILLARY NECROSIS IN CHILDHOOD. G. A. Stirling.
THE PATHOGENESIS OF BRONCHIAL CATARRH AND OF ACUTE AND CHRONIC BRONCHITIS. S. Engel.
FIBRINOLYSIS IN NORMAL PREGNANCY. J. J. Biezenski and H. C. Moore.
DIRECT COMPATIBILITY TESTING. N. A. F. Young.
HEREDITARY ELLIPTOCYTIC HAEMOLYTIC ANAEMIA. E. K. Blackburn, Arthur Jordan, W. J. Lytle, H. T. Swan, and G. R. Tudhope.
AN EVALUATION OF A NEW DIAGNOSTIC TEST FOR SYSTEMIC LUPUS ERYTHEMATOSUS. M. Wilkinson and E. G. Rees.
THE DIFFERENTIATION OF MYELOMATOSIS FROM OTHER CAUSES OF BONE MARROW PLASMACYTOSIS. W. A. Aherne.
THE NON-PROTEIN CONSTITUENTS OF THE PLASMA IN MYELOMATOSIS. N. H. Martin and H. Sculthorpe.
FRACTIONATION OF BENCE JONES PROTEIN BY STARCH GEL ELECTROPHORESIS. F. V. Flynn and Elizabeth A. Stow.
THE EFFECT OF SUNLIGHT AND TEMPERATURE ON THE REDOX POTENTIAL OF LIQUID MEDIA. S. Zador.
THE FATE OF GLUCOSAMINE HYDROCHLORIDE INJECTED INTRAVENOUSLY IN MAN. S. Weiden and J. J. Wood.
GALACTOSE AND GLUCOSE TOLERANCE IN NORMALS, THE OBESE, AND POST-GASTRECTOMY PATIENTS. S. Dische, W. P. Stamm, and R. B. Goudie.
KLEBSIELLA SEROTYPES IN INFECTIONS OF THE EAR AND UPPER RESPIRATORY TRACT. Samuel S. Epstein and I. Friedmann.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ● Application should be made first to the institution concerned.

Friday, August 8

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Dr. Ben H. Senturia (St. Louis): Diseases of the External Ear.

APPOINTMENTS

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—Keitha Corlett, M.B., Ch.B., M.R.C.P.Ed., D.C.H., and Lesley P. Leader, M.B., B.S., M.R.C.P., House-physicians; A. I. Munro, M.B., B.S., House-surgeon; E. P. Wilson, M.B., B.S., D.C.H., Assistant Medical Registrar; H. J. Weston, M.B., Ch.B., M.R.C.P., D.C.H., Resident Assistant Physician.

LIVERPOOL REGIONAL HOSPITAL BOARD.—H. Zabin, M.B., F.R.C.S.Ed., D.L.O., Part-time Consultant Ear, Nose, and Throat Surgeon, Walton Hospital.

MANCHESTER REGIONAL HOSPITAL BOARD.—W. M. C. Allen, M.B., Ch.B., D.M.R.D., Whole-time Consultant Radiologist, Preston and Chorley Group of Hospitals; W. M. Martin, M.B., B.Ch., D.A., Whole-time Assistant Anaesthetist, Burnley and District Group of Hospitals; P. H. D. Lewars, M.B., B.S., B.D.S., Senior Hospital Dental Officer, South Manchester Hospitals, etc.

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—G. H. Bancroft-Livingston, M.D., F.R.C.S., M.R.C.O.G., Consultant Obstetrician and Gynaecologist, Luton and Hitchin Groups of Hospitals; D. Ranger, M.B., B.S., F.R.C.S., Consultant Ear, Nose, and Throat Surgeon, Mount Vernon Hospital; Wendy E. Lewington, M.B., B.S., F.R.C.S., M.R.C.O.G., Consultant Obstetrician and Gynaecologist, Royal London Homoeopathic Hospital; Robert H. Gosling, M.D., D.P.M., and T. W. Goldblatt, M.B., B.Ch., D.P.M., Assistant Psychiatrists (S.H.M.O.), Tavistock Clinic.

QUINLAN, A. G., M.B., F.R.C.S., Consultant Orthopaedic Surgeon, Scarborough Group of Hospitals and Adela Shaw Orthopaedic Hospital, Kirby Moorside, Yorks.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—S. J. G. Spencer, D.M., D.P.M., Consultant Psychiatrist, Digby-Wonford Hospital, Exeter; J. F. Donovan, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, St. Lawrence's Hospital, Bodmin; J. L. Wilkins, M.B., B.S., Registrar in Paediatrics, South Devon and East Cornwall Hospital, Plymouth (joint appointment with the United Bristol Hospitals); A. J. Slim, M.R.C.S., L.R.C.P., D.A., Anaesthetic Registrar, Taunton and Somerset Hospital, Taunton; F. T. Page, M.D., M.R.C.P., Consultant Physician, Bristol Clinical Area.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Cole.—On July 20, 1958, to Margaret (formerly Whitham), M.B., Ch.B., and Brian W. Cole, M.R.C.S., L.R.C.P., of 439, Herries Road, Sheffield, Yorks, a son—Anthony Brian.

Smith.—On July 19, 1958, to Kathleen (formerly Turner), M.B., B.S., and Irvine Smith, F.R.C.S., at Burton-on-Trent, Staffs, a brother for Anne, Dorothy, and Geoffrey—Christopher Fredric.

Taylor.—On July 16, 1958, to Elizabeth (formerly Fowler), M.B., B.Chir., and Henry Taylor, of South Ridge, 32, Townsend Lane, Harpenden, Herts, a fourth daughter—Kitty Ruth.

MARRIAGES

Maisel—Douro-Dunlop.—On July 26, 1958, in London, Gerald Maisel, M.B., B.Chir., of Beverly Hills, California, U.S.A., to Laurette Adoré Douro-Dunlop, of London.

DEATHS

Bain.—On July 14, 1958, at West View, Arkendale, Yorks, Edward Walter Bain, F.R.C.S., late of Leeds, Yorks, aged 82.

Banbury.—On July 18, 1958, at his home, Heathdene, Bixley Road, Ipswich, Suffolk, Percy Banbury, M.R.C.S., L.R.C.P., D.P.M., aged 65.

Clarke.—On July 17, 1958, the result of an accident, Donald Reay Clarke, M.B., Ch.B., aged 63.

Cowin.—On July 11, 1958, at Highfield, Selborne Drive, Douglas, Isle of Man, Daniel Cowin, M.B., Ch.B., L.D.S. R.C.S.

Cullinan.—On July 13, 1958, at Fressingfield, Diss, Norfolk, John Henry Cullinan, M.R.C.S., L.R.C.P., aged 57.

Flett.—On July 25, 1958, at Peel Hospital, Galashiels, George Neil Flett, M.B., Ch.B., of Runic Cross, Innerleithen, Peeblesshire.

Gandy.—On July 21, 1958, Eric Worsley Gandy, O.B.E., V.D., M.R.C.S., L.R.C.P., D.A., of The Hill Top, Gipsy Hill, London, S.E.

Herriott.—On July 22, 1958, at St. Benet's Cottage, Titchfield Lane, Wickham, Gerard Michael Herriott, M.B., B.Ch.

Howie.—On July 14, 1958, following an operation, Nora Alice Howie, L.R.C.P.&S.Ed., L.R.F.P.S.

McDowall.—On July 19, 1958, at Dumfries Infirmary, William Andson McDowall, M.B., Ch.B.

Montgomery.—On July 17, 1958, at 588, Woolwich Road, Charlton, London, S.E., John Montgomery, M.B., Ch.B.

Potterton.—On July 12, 1958, De Courcy Potterton, L.R.C.P.&S.I., aged 86.

Stevenson.—On July 13, 1958, John Black Stevenson, *M.C.*, M.B., Ch.B., of 88, Brighton Road, South Croydon, Surrey, aged 77.

Thomas.—On July 12, 1958, at the Radcliffe Infirmary, Oxford, Thomas Ben Thomas, M.R.C.S., L.R.C.P., of "Hillside," Eden Avenue, Swansea.

Waller.—On July 1, 1958, Hugh Bevan Waller, L.M.S.S.A., of 153, Seven Sisters Road, London, N., aged 75.

Warner.—On July 15, at Cambridge, Charles Mark Ernest Warner, M.B.E., M.R.C.S., L.R.C.P., late of Upper Assam, Bombay, and Calcutta, India.

Way.—On July 15, 1958, at Pyle, Chale, Isle of Wight, Leslie Ferguson Kennedy Way, D.S.O., M.R.C.S., L.R.C.P.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Acrylic Lens Implants

Q.—*What are the arguments for and against the implantation of intraocular acrylic lenses?*

A.—After extraction of a cataract the refraction of the eye is usually restored by a powerful spectacle lens. This lens, of approximately 11 dioptres, necessarily placed several millimetres anterior to the cornea, may provide excellent central vision but with several optical defects. Oblique views produce distortion and apparent displacement of objects so that the effective visual field is restricted, and, since the lens magnifies the retinal image by about one-third, the sight is far from natural even though central acuity may be normal. When the other eye retains good sight the two eyes, if focused with appropriate spectacles, cannot be used together because of the disparity of the retinal images and the prismatic effect of oblique views. The defects of aphakia, other than loss of accommodation, can be overcome by inserting an artificial lens within the eye either behind or in front of the iris.

Intraocular acrylic lenses are now known to be tolerated and to provide good sight for at least eight years. There is no evidence of tissue sensitivity to the acrylic material, though there may be to other matter, including chemical sterilizers which have not been adequately removed. Operative hazards are obviously increased to some degree by the surgical complexity of the procedure, whether the operation is completed in one stage or two, and convalescence is often slow. An intraocular lens gives great benefit in uniocular cataract because it enables both eyes to be used together. But intraocular lenses should not at present be advised for bilateral cataract, though a number of patients now have acrylic lenses in both eyes because cataract developed in the second some years after the first.

Trichostrongylus Colubriformis Infection

Q.—*Is Trichostrongylus colubriformis a saprophyte or a parasite in man? What is the treatment?*

A.—*Trichostrongylus colubriformis* is a parasite which seldom produces severe symptoms in man but may occasionally do so. It normally inhabits the intestines of sheep and goats, but human infections have been reported from Japan, India, Egypt, Central Africa, and the United States of America. In many cases, particularly in those in which the infection is light, symptoms are absent, but anaemia, occasionally severe, may be produced. The treatment is the same as for infection with the common hookworm *Ankylostoma duodenale*, and the most effective remedy for it is hexylresorcinol. This should be administered in rice-paper cachets, and for adults the dose is 1 g. Unless rice-paper cachets are used the drug may not be liberated from its container and hence act on the worms until it has passed the duodenum. For those too young to swallow cachets tetrachlorethylene administered in an emulsion with mucilage and in appropriate proportions of the adult dose of 4 ml. is also satisfactory. Patients should be treated in the morning, food having been withheld since 4 p.m. on the previous day, and half an hour after treatment a saline purge should be administered. Anaemia, when present, is usually of the iron-deficiency type and should be treated accordingly. In the absence of symptoms and of anaemia, treatment is not necessary.

"Bees Wine"

Q.—*Is the liquid strained off from the "ginger beer plant" (Saccharomyces pyriformis), to which sugar and powdered ginger has been added daily for three weeks, harmful to health?*

A.—Various authorities over more than sixty years have found that the "ginger beer plant," sometimes referred to as the plant producing "bees wine" or "beasty beer," is a "consortium" made up of certain yeasts and bacteria. The yeast has mostly been described as either *Saccharomyces pyriformis* or a form of ordinary brewers' or bakers' yeast. The bacterium was at one time referred to as *Bacterium vermiforme*, but more recently the spongy masses or "bees" have been found to contain *Lactobacillus* sp. So far as can be ascertained from the scientific literature, there is no reason to suppose that any of these organisms are harmful under ordinary conditions. Furthermore, to the best of our knowledge there are no special risks to health from the produce of the ginger beer plant as distinct from the produce of more familiar alcoholic fermentations. Indeed, the slight acidity of the beverage due to the organisms employed makes the risk of harmful infection relatively small as compared with that of various other foods and drinks.

Treatment of Schistosomiasis

Q.—*What are the comparative advantages of sodium antimonyl tartrate, sodium antimonyl gluconate, stibophen, and lucanthone in the treatment of schistosomiasis?*

A.—The principal advantage of sodium antimonyl tartrate is that it is the most effective drug known for the eradication of schistosomiasis, but its main disadvantage is that it is relatively toxic, causing nausea, vomiting, and lassitude, so that treatment in hospital with close medical supervision is necessary. Treatment with sodium antimonyl gluconate gives rise to very few side-effects, and may be given to out-patients to control symptoms and to reduce the worm load among communities in the tropics. Its main disadvantage, however, is its relative ineffectiveness in eradicating the disease, persistence of some symptoms after treatment occurring in approximately twice as many patients as after a course of treatment with sodium antimonyl tartrate. A further disadvantage is that it must be administered intravenously. The considerations applicable to it also apply to stibophen, with the single exception that stibophen may be given intramuscularly. The principal advantage of lucanthone is that it may be administered orally, but its disadvantages are that it is less effective than either sodium antimonyl gluconate or stibophen in reducing symptoms and the worm load, and its administration is associated with very marked nausea and vomiting, so that it is with difficulty that patients can be persuaded to complete a course of treatment with it.

Effectiveness of Pertussis Vaccine

Q.—*What proportion of children who have been immunized against pertussis develop the disease later?*

A.—The most authoritative answer is to be found in the report to the whooping-cough immunization committee of the Medical Research Council.[1] Although the main purpose of the report was to compare the protective potency of various pertussis vaccines, it was possible in the course of the studies to deduce the absolute value of pertussis vaccination. I quote from the report: "Taking all vaccines together, the attack rate [among the vaccinated] in 801 home exposures was 14%, ranging from 4 to 29% (Table VII). In the controlled trials reported previously (M.R.C., 1951)[2] the attack rate in the control unvaccinated groups was 87%."

On the duration of protection conferred by the vaccine, I quote again from the report: "An analysis was made which showed that during the period of observation there

was no waning in the degree of immunity afforded by the vaccines. Taking all the vaccines together, the attack rates in 'home exposures' at six-monthly intervals after vaccination showed no evidence of increasing two and a half to three years after vaccination (Table VIII)." I know of no reliable figures, based on large numbers, where the observation of the vaccinated was continued for more than three years.

REFERENCES
[1] Medical Research Council, *Brit. med. J.*, 1956, **2**, 454.
[2] —— ibid., 1951, **1**, 1463.

Diagnosis of Whooping-cough

Q.—*What are the latest methods of diagnosing whooping-cough?*

A.—The diagnosis of whooping-cough before the paroxysms or when these are atypical is best established by isolation of the *Haemophilus pertussis* on a cough plate or from a pernasal swab. If there is no spontaneous cough one should be elicited; a simple and infallible way of doing this is described in detail in the *British Encyclopaedia of Medical Practice* in the chapter on whooping-cough.[1] In general practice a pernasal swab is preferable to a cough plate, but the swab must be taken immediately after a bout of coughing, passed along the floor of the nose straight back on the nasopharynx, and cultured the same day. The culture medium should contain 50% of fresh blood, half a unit of penicillin per millilitre, and should not be more than eight days old. A definite result can be obtained in four days and will be found positive in 95% of cases in the first and second weeks of the disease. The percentage of positive results diminishes rapidly in the third and fourth weeks, but the clinical diagnosis is usually obvious at this stage.

A total leucocyte count of over 20,000 cells, with 70% or more of lymphocytes, can help in confirming a suspected attack of whooping-cough, but by itself is not diagnostic. A high lymphocyte count may be seen in children with other infections, and it can follow the administration of pertussis vaccine. Though areas of pulmonary collapse are often a complication of whooping-cough, there is no diagnostic radiological picture. Enlarged hilar glands are not due to whooping-cough. Positive complement-fixation test and the presence of specific agglutinins occur too late in the disease to be of much practical value in diagnosis.

REFERENCE
[1] Laurent, L. J. M., in *British Encyclopaedia of Medical Practice*, 1952, edited by Lord Horder, vol. 12, p. 693. Butterworth, London.

Pulsus Paradoxus

Q.—*What is the explanation of the phenomenon of pulsus paradoxus in constrictive pericarditis?*

A.—When the diastolic filling of the heart is restricted by pericardial effusion or constriction of the pericardial sac, the pulse weakens on inspiration. As a result of the restricted inflow the output falls and a weak pulse is easily felt with the finger on inspiration.

Ascorbic Acid Prophylaxis in Toxic Drug Therapy

Q.—*It has been claimed[1] that liberal dosage with ascorbic acid, together with small oral doses of a ferrous preparation to catalyse the redux activity of the vitamin, counteracts the harmful side-effects of phenylbutazone therapy. Can this claim be taken as settled?*

A.—To settle a claim that a combination of ascorbic acid in large amount together with a ferrous preparation would counteract such effects of phenylbutazone as agranulocytosis and aplastic anaemia would obviously be a major scientific undertaking. There is evidence that ascorbic acid is of value in benzene poisoning, which is an industrial hazard, but there has been no formal investigation of its action in agranulocytosis. One serious difficulty is that there is no method of producing agranulocytosis experimentally which works in more than a proportion of animals. Daft *et al.*[2] produced granulocytopenia in rats by including 1% thiourea in the diet, and a test of the value of ascorbic acid could be made by using such animals. It is hard to suppose that conclusive evidence of the value of ascorbic acid could be obtained from patients. The evidence obtained by Drummond[3] appears to be complicated by the administration of cortical hormones as well as ascorbic acid. In a later paper by Drummond and Atlas[4] two further cases were described in which the leucopenia due to phenylbutazone was counteracted by giving doses of vitamin C such as 250 mg. twice daily and a ferrous iron preparation three times a day.

REFERENCES
[1] Drummond, J., *Brit. med. J.*, 1957, **2**, 1546.
[2] Daft, F. S., Kornberg, A., Ashburn, L. L., and Sebrell, W. H., *Proc. Soc. exp. Biol.*, 1946, **61**, 154.
[3] Drummond, J., *S. Afr. med. J.*, 1950, **24**, 975.
[4] —— and Atlas, L., ibid., 1953, **27**, 997.

Infra-red Fire

Q.—*Is the use of an infra-red electric fire for heating a room detrimental to health?*

A.—No; an electric fire emits infra-red rays and some visible rays. The effect of the former is only to heat, and, provided ordinary precautions against burning are taken, there can be no possible detriment to health.

NOTES AND COMMENTS

"Wind."—Dr. J. A. RANKIN (Reading) writes: I was interested to read the answer on the above subject ("Any Questions?" June 28, p. 1556). The gas content of the bowel is of interest to me in radiodiagnosis, and recently I carried out some investigations from this point of view. A series of patients was given a course of digestive enzyme therapy and their bowel gas content compared with that in a similar control series. The faecal residues were also sent for analysis. The results showed that the treated cases were much freer of bowel gas, and that digestion was more complete. It would appear, therefore, that it is possible to influence bowel gas formation by digestive enzyme therapy, at the same time improving digestive processes, and I feel sure that clinical investigation of such enzyme therapy would be most rewarding.

OUR EXPERT replies: It is not stated how the bowel gas content was measured. However, it is understood that *x*-ray films of the abdomen were clearer of gas shadows on this treatment than without it. Frankly, caution is needed in interpreting results in this type of work. It is difficult to understand how digestive enzymes could reduce bowel gas, for some gas is produced during digestion in the gut. In any case upwards of half the gas in the gut is swallowed nitrogen, and it is difficult to understand how this could be influenced in the way suggested.

Correction.—In the report of Professor G. W. A. Dick's remarks at the meeting of the Section of Medicine at Birmingham (*Journal*, July 26, p. 222) the words "some clinical infections" were printed instead of "subclinical infection."

Collected Articles from the "British Medical Journal"

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